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GLAUCOMA DETECTION IN AN OUTPATIENT DEPARTMENT

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Routine tonometry led to the recognition of glaucoma in 49 out of 1,210 outpatients over 40 years of age tested in a glaucoma detection program of a teaching hospital. For the determination of ocular tension a local anesthetic must be instilled in each eye. The tonometer, with certain precautions to avoid transfer of infections, is placed directly on each cornea. Additional data were furnished by a water provocative test, a tolazoline test, conventional testing of the central and peripheral visual fields, and the new Harrington-Flocks test. The last-named test measures central visual fields and is adapted to mass screening because it eliminates difficulties about the central fixation point by using brief flashes of ultraviolet radiation to illuminate the test pattern. The detection of defects in the visual field was thus facilitated, but the differences observed between the glaucomatous and nonglaucomatous eyes were more striking in the water provocative and tolazoline tests and in disk examinations than in any of the methods of campimetry.

GLAUCOMA is an important and common eye disease which has as its characteristic sign an increase of intraocular tension and may affect one or both eyes. It occurs most commonly in individuals over 40 years of age, and it is somewhat more common among women than men. This increased intraocular pressure is produced by an interference with drainage of the aqueous fluid, the cause of which is uncertain; it gradually destroys the function of the retina and optic nerve by exerting an outward thrust on the optic nerve head at the point of its entrance to the eye. By the time anatomic changes in these structures have taken place, much useful vision has been lost at the sides of the visual fields and through enlargement of the blind spot.

The three most common types of glaucoma found among adults are acute congestive, chronic simple, and secondary. In acute glaucoma, the symptoms of severe pain and cloudy vision produce so much discomfort that medical attention usually is sought promptly. Chronic simple glaucoma, which is far more prevalent than the acute type, is the most dangerous type, since there is a gradual painless loss of peripheral vision of which the person may be completely unaware. Glasses appear to need frequent changing, but new glasses do not relieve the patient's occasional vague headaches and, at

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certain times, blurred or foggy vision. Secondary glaucoma, as the term implies, develops either as the result of other ocular disease or after injury.

Early detection of glaucoma has long been recognized as the most important measure for preventing loss of vision from this disease, because early treatment greatly increases the likelihood of controlling intraocular pressure. It is estimated that in the United States 42,000 men and women are blind from bilateral glaucoma and that an additional 150,000 are blind in one eye. Thus, at present, one out of eight blind persons has lost sight from glaucoma. The annual incidence of blindness from this cause is estimated at 3,500 cases, and it is further estimated that one million persons over 40 years of age in the United States have unrecognized glaucoma. Due to the increase in the span of life, glaucoma is becoming more common, and failure to recognize or diagnose this disorder in its early stages is particularly disastrous in a disease process where vision, once lost, cannot be restored. This is especially tragic because effective treatment, with normalization of intraocular pressure by medical or surgical means, can preserve vision for the lifetime of the individual. It is for this reason that early detection is important, and this requires that tonometry be made a part of every general physical examination in persons over 40 years of age, even in the absence of eye complaints.

Criteria for Diagnosis

One of the simplest methods of recognizing glaucoma in its early stages is the measurement of intraocular pressure with a tonometer. Physicians can be taught to use this instrument skillfully after brief instruction. Measurement of intraocular pressure requires less time and no greater aptitude than obtaining the blood pressure. The routine determination of intraocular pressure at regular intervals in all patients over the age of 40 would be a major step toward avoiding much of the blindness resulting from glaucoma.

The purpose of the study reported here has been to determine if routine tonometry of all patients over 40 years of age attending the various clinics of the John Gaston Hospital outpatient department would permit an early diagnosis of glaucoma to be made in a significant number of patients before they are aware of any visual loss. During the same period (September, 1956, to February, 1957), all patients over 40 years of age admitted to the eye clinic of this hospital's outpatient department for any reason were similarly tested by medical students, all of whom had received instructions in this procedure. Their results were checked by the resident staff. Approximately 80% of the patients attending these clinics are Negro.

It was originally planned to include for comparison a large group of healthy persons as a control group by determining ocular tensions in persons over 40 years of age applying to the outpatient department for an employment health card. This plan was discontinued, because only a small proportion of this group was found to be over 40 years of age and it was considered to be more productive to rotate testing personnel through the various outpatient clinics than to wait for health-card applicants to present themselves. However, results will be reported on persons admitted to the eye clinic for refraction only, who were subjected to the various tests under study, and also on those with initially elevated ocular tensions whose subsequent tests for glaucoma were found to be negative but who were subjected to a complete evaluation before this negative status was evident. These constitute control groups for comparison purposes and will be subsequently referred to as "normal" and "non-glaucoma" groups respectively.

The ocular tension determinations obtained in the various outpatient clinics were recorded by a nurse who had received special training in this procedure. Any patient found to have an ocular tension of over 23 mm. Hg by the Schiøtz tonometer (based on the 1954 Schiøtz-Friedenweld calibration) was referred to the eye clinic and rechecked there by the resident in ophthalmology. Ocular tensions were also routinely determined in all patients in the eye clinic by medical students. Inflamed eyes were checked by the resident before either the nurse or the medical students were allowed to measure the ocular tension to avoid undesirable trauma and to prevent the tonometers from being contaminated by an infectious conjunctivitis. All patients with ocular tensions of over 23 mm. Hg, but not high enough to indicate obvious glaucoma (i. e., 35 or 40 mm. Hg), were scheduled for water provocative and tolazoline (Priscoline) hydrochloride tests. Regardless of whether these latter tests were positive, the optic disks were examined and peripheral, central, and Harrington-Flocks field tests were performed on each person suspected of having glaucoma before the diagnosis was considered to be definitely positive or negative.

In this study, the criteria for the diagnosis of glaucoma, in order of importance, thus included (1) a tension elevation of over 23 mm. Hg, or more than 4 mm. Hg difference in pressure between the two eyes, or a variation of 5 mm. Hg or more in the same eye during the day; (2) abnormalities in the water provocative and/or tolazoline tests; (3) the abnormal appearance of the disks on ophthalmoscopic examination; and (4) a constriction of central and peripheral fields not accounted for by some other disease.

Techniques of Testing

Ocular Tension.—Before the determination of ocular tension, the patient is placed in the reclining position and two drops of 0.5% tetracaine (Pontocaine) hydrochloride solution are instilled in each eye twice, about one minute apart. The patient is requested to look straight ahead, the tonometer is

placed directly on each cornea, and the reading is obtained for each eye. One drop of nitrofurazone (Furacin), a disinfectant eye drop with a wide bactericidal spectrum, is then placed in each eye. The tonometer foot plate is cleansed with an alcohol sponge and dried with cotton before being placed on the next patient's eye.

In testing and retesting approximately 1,200 patients (2,400 eyes) from the various outpatient clinics, we discovered no allergic reactions to the tetracaine instilled to anesthetize the cornea and only 17 corneas were scratched by a tonometer to a sufficient degree to require treatment. All of these corneal abrasions were diagnosed by fluorescein stain as soon as the patient complained of ocular pain, which usually occurred before the end of the examination, and were treated with antiseptic drops and a dressing to prevent infection. Patients were cautioned not to rub the eyes for at least one hour after the examination to avoid trauma to the anesthetized cornea. An allergic reaction to nitrofurazone was observed in only one patient in our study. In such a large series of examinations performed by a nurse, this lack of serious ocular damage to any patient indicates that ocular tension determinations can safely be entrusted to trained medical personnel.

On each patient showing a tension elevation, an index card was filled out with his name, clinic number, address, age, sex, race, and any information which would aid in establishing a diagnosis for or against glaucoma. This was found to greatly simplify the accumulation of data for periodic reports and made the data much easier to compile for final analysis.

Water Provocative Test.—When the water provocative test is performed, the patient suspected of having glaucoma is required to have eaten or drunk nothing since midnight the night before the test. Ocular tension is recorded, and the patient is given a liter of water to drink as rapidly as possible, preferably in two to four minutes. Ocular tension is then recorded every 15 minutes for four times. The tension determination is repeated a fifth time if it was still elevated the fourth time, i. e., one hour after the initial tension measurement was obtained prior to the drinking of water. We considered an elevation of 6 mm. Hg in either eye after drinking water to be positive for the water provocative test.

This test is based on the following principle. Many glaucomatous eyes, as compared to normal eyes, have a decrease in outflow facility. A normal eye can carry off a sudden increase in aqueous volume, but a glaucomatous eye, due to decreased aqueous outflow, develops a temporary elevation in tension which has been provoked by the water drinking. This test is a deliberate effort to precipitate a tension elevation, if decreased aqueous outflow is indeed present, in order to help establish the diagnosis.

Tolazoline Test.—The tolazoline test is carried out as follows. The patient is permitted to eat and drink before the test. A control tension determination is done, after which 1 cc. of tolazoline (10 mg. in 1 cc. of water) is injected subconjunctivally in each eye. Ocular tension determinations are then done every 15 minutes for one hour. A rise in pressure of 9 mm. Hg in either eye was considered in this study to be positive for this test. In the series of 334 eyes tested, no allergic reactions to tolazoline were noted. The tolazoline test is based on the action of tolazoline as a dilator of blood vessels which brings more body fluids into the area where it is injected. Here again, the glaucomatous eye cannot carry off the extra fluid as well as the normal eye. The water provocative test is a time-honored test, whereas the tolazoline test is relatively new.[1]

Central and Peripheral Visual Fields.—Tests of central and peripheral visual fields were performed in the usual manner, with use of the tangent screen with hand targets. For a central and peripheral field examination to be satisfactory, the patient must be cooperative and have sufficient understanding to maintain his gaze on the central fixation point. Also, his vision must be sufficiently adequate to see the target, which, for the diagnosis to be definitive, should be the smallest size that can be seen clearly. The hazard of relying entirely on field changes in diagnosing glaucoma lies in the fact that other eye conditions besides glaucoma may cause vision loss in the central and peripheral fields and that not every patient can understand the purpose and procedure of the test sufficiently to be cooperative.

The Harrington-Flocks Screening Test.—A new procedure which offers promise of value as a method of screening for glaucoma is the multiple-pattern method of visual field testing described by Harrington and Flocks.[2] In this test, a series of 10 cards with abstract patterns of lines, dots, and crosses is used. A black central fixation point is visible with ordinary light, but each pattern can be seen only when illuminated with a flash of ultraviolet light for one-fourth of a second. The duration of the flash gives an adequate stimulus to extrafoveal vision but is too short to permit a shift of fixation. Errors in describing any card can be recorded on a composite control and field defects quickly noted. Because a technician can be trained to use this rapid test and no medication is needed, the method deserves further experimental use. It is a test of central fields only.

Analysis of Data

Results of the Detection Program.—Of 1,210 persons receiving the tonometer test at the outpatient clinics (excluding the eye clinic) over a period of six months, 313 (25.8%) were found to have elevated ocular tension. Of these it was possible to secure retests on 259 individuals, of whom 119

(9.8% of the number receiving the initial test) showed elevated tension on the second test. A diagnosis of newly discovered glaucoma was ultimately made, with use of the tests and criteria described above, in 49 patients (4% of the number originally tested). The diagnosis of borderline glaucoma was made in an additional 14 patients (1.1%). During the same period, 46 cases of glaucoma were diagnosed in individuals who came to the eye clinic. The latter group consisted for the most part of late cases with advanced visual loss, while most of the patients in the former group had no subjective visual loss when tested. Further comparison of these two groups will be made later.

Comparison of Tests in Four Groups.—The table shows a comparison of findings in relation to various eye-testing procedures employed in the following four groups: (1) patients with glaucoma discovered in the detection program; (2) patients with glaucoma diagnosed in the eye clinic to which they had come because of symptoms; (3) patients whose condition was classified as nonglaucoma but in whom elevation of ocular tension on the initial test and retest was shown; and (4) normal individuals, usually applying for refraction, whose initial ocular tension was within normal limits or whose tension was initially elevated but normal on retest.

Abnormal Findings with Various Tests in Four Groups

	New Glaucoma				Non-glaucoma		Normal	
	OPD		Eye Clinic					
Test	No.	%	No.	%	No.	%	No.	%
Water provocative	83	39.0	54	61.1	102	14.7	73	17.8
Tolazoline	66	45.4	48	47.9	78	12.8	57	19.3
Optic disk	83	30.1	71	42.3	90	2.2	81	3.7
Field								
Central	79	57.0	67	86.6	68	64.7	45	37.8
Peripheral	80	63.7	68	73.5	66	57.6	47	42.5
Central (Harrington-Flocks[a])	79	41.8	64	54.7	80	30.0	70	20.2

The data in this table represent findings in eyes examined, since abnormal findings were frequently found in one eye only. It will be noted that the percentages of eyes showing abnormality in the water provocative, tolazoline, and optic disk examinations in the "new glaucoma" groups are significantly higher than the percentages in the "nonglaucoma" and "normal" categories. Within the new glaucoma category, the outpatient department and eye clinic groups did not differ significantly in the percentages of eyes found abnormal with these tests. For example, the percentage of glaucomatous eyes showing abnormal results with the water provocative test in the outpatient department and eye clinic were 39% and 61.1%, respectively, whereas in the nonglaucoma and normal groups these percentages were 14.7 and 17.8 respectively. These similarities follow throughout.

A comparison of abnormalities in field of vision tests in the above four groups reveals less striking differences between the glaucoma and nonglaucoma groups. For the newly discovered glaucomatous eyes it will be noted that the most striking difference in percentage is seen in the test for central field vision (tangent screen). Fifty-seven per cent of the glaucomatous eyes in the outpatient department group and 86.6% of those in the eye clinic group showed abnormality in this test, a difference which is statistically significant ($p=0.05$) and seems to indicate that loss of central vision is readily noted by the patient, once it occurs, and plays an important role in bringing him to the eye clinic, where diagnosis of glaucoma is subsequently made. The percentage of abnormal central fields (37.8%) was significantly lower in the normal group, but was surprisingly high (64.7%) in the nonglaucoma group. This probably reflects the fact that many of the patients in the latter group were suffering from nonglaucomatous eye conditions which affected the central field of vision, such as diabetic and hypertensive retinopathy, macular degeneration, chorioretinitis, and cataracts. This same factor probably accounts for the fact that percentage of peripheral field abnormalities in the nonglaucoma group was not significantly lower than that found in the glaucoma group. However, the normal group showed a significantly lower percentage of abnormalities in the peripheral fields when compared to the glaucoma groups. Inability of patients to comprehend and to cooperate probably accounted for many of the abnormal results recorded in central and peripheral field tests in the normal group. Strictly speaking, the latter does not consist of normal individuals, since many members of this group had been selected for further study by virtue of the initial elevation of ocular tension.

The percentage of eyes in which results of the Harrington-Flocks test were abnormal was higher (54.7%) in the eye clinic group than in the outpatient department group (41.8%). This difference is not statistically significant. The percentage of eyes showing abnormal results with the Harrington-Flocks test in the normal group was significantly lower than the percentage that was found in the groups with glaucoma. Since the Harrington-Flocks test measures central visual fields only, it is of interest that the percentage of normal eyes showing a positive test (20.2%) was significantly lower than the percentage (37.8%) of normal eyes which were classified abnormal when the standard tangent screen with hand targets was employed. A possible explanation for this difference in specificity is that less fatigue is associated with the Harrington-Flocks test than is the case with the tangent screen test. This fatigue may be responsible for abnormal readings in individuals actually possessing normal central fields of vision. This may be an important consideration in connection with the use of the Harrington-Flocks test in mass screening for loss of central fields. The outpatient department group simulates best the types of individuals who would

be encountered in a mass screening program reaching those without manifest eye symptoms. It will be noted that in this group the sensitivity of the Harrington-Flocks test was 15.2% lower than that of the central visual field test with the tangent screen. This lower degree of sensitivity in glaucomatous eyes, however, may be more than compensated for by the increased specificity, referred to above, of the Harrington-Flocks test as observed in normal eyes. This deserves further investigation, in view of the simplicity of this test.

Summary

A glaucoma detection program was instituted in the outpatient department of a teaching hospital. Routine tonometry of all persons over 40 years of age newly admitted to the outpatient department were performed during a six-month period. Of 1,210 patients tested, 49 (4%) were ultimately found to have unrecognized glaucoma. Had all patients initially tested returned for completion of the examination, the yield of newly discovered cases of glaucoma would have been even higher.

During the same period of time, 46 cases of glaucoma were diagnosed in individuals who came to the eye clinic of the outpatient department. The proportion of this group manifesting abnormal signs and symptoms was greater than that in persons with glaucoma found in the detection program, indicating that the former group represented patients in a more advanced stage of the disease.

Differences observed between the glaucomatous and nonglaucomatous eyes were most striking in the water provocative and tolazoline tests and in disk examinations and less notable in the central, peripheral, and Harrington-Flocks field of vision tests. The Harrington-Flocks visual screening test shows promise as an instrument for mass screening for defects in central visual field in view of its greater specificity and its reasonable sensitivity when compared to tangent screen tests which are more time consuming and fatigue producing.

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STUDY OF COLON BY USE OF HIGH-KILOVOLTAGE SPOT-COMPRESSION TECHNIQUE

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Cancer of the colon and rectum is currently responsible for approximately 17% of all deaths due to neoplasm in the United States. Despite marked advances in the surgical treatment of this lesion, a significant reduction in the number of deaths due to carcinoma of the colon and rectum can be achieved only through the early detection and treatment of the precancerous or early malignant lesions of the large intestine.

The prevailing concept that polypoid lesions of the colon are potentially malignant necessitates the use of a simple, accurate, routine method for their detection, whether the patient is symptomatic or

From the Division of Radiology, Grace Hospital.
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There is a prevailing concept that polypoid lesions of the colon are potentially malignant. Most radiologists rely on the double-contrast enema for the detection of colonic polyps. The new, simple, and most accurate method devised combines the use of large-field spot-compression radiography with high kilovoltage. The problem arising from this approach is no longer one of detection but rather the management of these lesions. A more conservative attitude toward very small, readily observable polyps seems justified.

asymptomatic. Until recently detection of colonic polyps beyond the reach of the endoscope was possible only with highly specialized roentgenographic studies which were generally carried out only in highly selected patients. Most radiologists rely on the double-contrast enema for the detection of colonic polyps; however, they openly admit the inadequacies and difficulties of this method.

We have evaluated all known techniques and have decided that the simplest and most accurate method available combines the use of large-field spot-compression radiography with high kilovoltage. This is complemented with routine high-kilovoltage enema films so that a detailed search for polyps is made on the routine examination of the colon in every patient. We have used this method routinely for 15 months and have been successful in detecting lesions as small as 2 mm. in size. In most of these cases other accepted techniques (high-kilovoltage studies, double-contrast studies, and postexpulsion roentgenograms) were unsuccessful in the detection of these small lesions as well as occasional larger lesions.

Evolution of Contrast Studies of Colon, with Particular Emphasis on Detection of Polypoid Lesions

Almost immediately after Roentgen announced his discovery of the x-ray, numerous investigators attempted in various ways to delineate the internal structures in an effort to diagnose abnormalities of the internal organs. The original examination of the colon by x-ray entailed filling of the colon with opaque medium (bismuth or barium), thus permitting the examiner to observe or record the normal or abnormal silhouettes of the colon. Since this method of examination allowed only the detection of gross pathological changes, it can readily be understood why numerous modifications have been introduced. It was not until the use of spot-compression roentgenography and the study of the mucosal pattern of the colon on the postexpulsion roentgenogram [1] that an occasional, smaller intraluminal polypoid lesion was detected.

Compression techniques consist of the application of pressure over the barium-filled colon, manually or by means of cones of various sizes and shapes, in an effort to detect constant radiolucent defects within the lumen of the colon. We have utilized compression techniques with spot radiography at the time of fluoroscopy since 1951 in our routine examination of the colon in an effort to detect intraluminal polypoid lesions. We were successful on a great many occasions in detecting lesions 7 mm. in size and larger. As with the double-contrast technique, considerable experience and skill on the part of the examiner is required for carrying out this study with any degree of success. With this approach, however, intraluminal lesions are sought for on the initial examination, and the demonstration of disease states is usually much more convincing than with the double-contrast study.

The double-contrast study was introduced by Fischer in 1923 and later modified by Weber, Moreton, and others.[2] This provided a greatly improved technique for the detection of intraluminal lesions. Most radiologists are openly critical of this method because of various inherent deficiencies.

In 1951 Gianturco [3] introduced the high-kilovoltage study of the barium-filled colon. This provided a simple, routine method for evaluation of the colon including the detection of a significant percentage of polypoid lesions on the initial, routine study. In his series of cases he reports an incidence of 2.37% polypoid lesions.

Equipment enabling us to utilize high-kilovoltage techniques was installed at Grace Hospital, Northwestern Branch, in 1953. Wietersen's studies [4] with this equipment confirmed Gianturco's findings. However, with compression techniques, we were still occasionally detecting polyps which, in some instances, could not be detected accurately, if at all, on routine high-kilovoltage films or on double-contrast studies (fig. 1 and 2).

At this time, since no individual method appeared completely foolproof, we decided to utilize a combined approach (spot-compression studies at the time of fluoroscopy, high-kilovoltage enema films, postexpulsion roentgenogram, and barium air-contrast study) in an effort to optimally evaluate those patients who were polyp suspects clinically or in whom polypoid lesions were detected or suspected on the premise of the initial barium examination.

A technique allowing us to utilize all of these methods was devised and applied during the years 1953-1955. The purpose of this intensive combined approach was threefold: 1. It allowed us to be extremely exact and accurate in our evaluation of the colon, especially regarding the absence or presence of polypoid lesions. 2. The over-all cost of the study to the patient was greatly reduced, since we were able in almost all instances to establish the presence of polyps in two sessions; obviously this also reduced greatly the discomforts of preparation which the patient had to undergo, as additional reexaminations were not necessary. 3. This approach has allowed us to evaluate critically and compare all methods currently applied by the radiologist for the evaluation of the colon, especially for polypoid lesions.

Our conclusions in this regard are as follows:

1. Accurate fluoroscopic control is of immeasurable value for evaluation of lesions of the gastrointestinal tract, especially when proper compression techniques are applied, whether it be for the detection of polypoid lesions or for demonstration of mucosal abnormality such as ulceration. Persistent intraluminal defects or deformities visualized

under the fluoroscope and the image recorded on the spot roentgenograms produces in many instances incontrovertible evidence. Obviously there is a limit to this approach, even with the use of image intensification devices. Smaller lesions (less

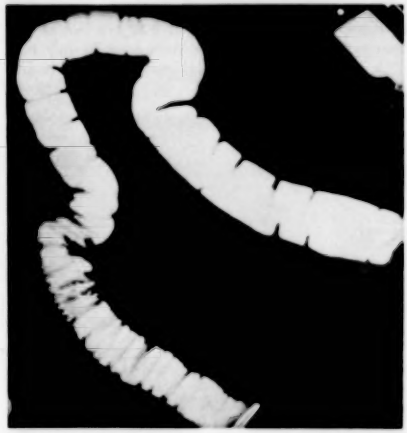

Fig. 1.—Roentgenogram of surgical specimen filled with barium in masonite phantom. Note defect is barely perceptible when exposure is made utilizing 120 kv.

than 7 mm. to 10 mm. in size) cannot ordinarily be seen under the fluoroscope except in unusual circumstances, and even larger lesions may be missed. The results will be proportionate to the skill and experience of the observer; however, basically, this technique is easily mastered. Let us stress once again the value of the compression approach since by this method the constancy and frequency and the exact anatomic or pathological characteristics of the defect can be identified, occasionally even in the presence of considerable fecal accumulation throughout the intestine.

2. The high-kilovoltage enema study is a simple, accurate, and an easily reproducible method for evaluation of the colon; however is not completely foolproof. In some instances in our experience the presence of fecal matter, areas of colonic spasm, technical errors (improper positioning of the patient by the technician, thus missing a critical area, etc.) as well as insufficient penetration of the barium-filled ascending colon or larger, more redundant loops of colon have failed to identify either lesions already shown to exist by compression techniques or those suspected from study of the postexpulsion roentgenogram. Although Gianturco stresses the value of visualizing one barium-filled loop through other overlapping loops, he does not stress the ineffectiveness of detecting smaller lesions in these loops.

3. Our experiences have confirmed the generally accepted and prevailing opinion that the double-contrast study is inadequate as routine procedure for evaluation of the colon. Even if one is to selectively apply this method only to patients suspected of having polyps, many inadequacies still exist. This statement is premised not only on our personal experiences but, more importantly, on the experiences of innumerable radiologists with whom this problem has been discussed at various meetings where our material has been exhibited. We have proved time and time again that double-contrast studies have failed to reveal lesions conclusively localized by other methods. We would like to add that the proponents of the double-contrast study actually prefer to carry out this procedure only if the patient is a polyp suspect clinically (polyps at sigmoidoscopy or unexplained gastrointestinal bleeding), thus making little or no effort at detection of these lesions in asymptomatic individuals who, nevertheless, may harbor such lesions.

Let us repeat then—we have evaluated all known techniques in a series of approximately 100 proved cases of polypoid lesions of the colon. Lesions detected by compression techniques or on high-kilovoltage enema studies were not infrequently demonstrated in a very equivocal fashion on

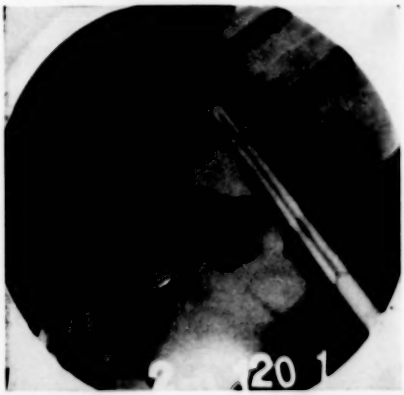

Fig. 2.—Same area as in figure 1, exposure made with compression at 120 kv.

double-contrast studies with the observer knowing exactly where to look for the lesion. At times, extremely high-quality double-contrast films did not localize the lesions at all, some of which were as large as 2.5 cm. in diameter. This, of course,

does not include the large percentage of cases in which double-contrast studies were worthless for one reason or another.

It was this dissatisfaction with the double-contrast enema, as well as our awareness of some of the deficiencies in the high-kilovoltage enema study, that led us to experiment with the effects of large-field compression spot films in the high-kilovoltage range. We felt that optimal detection, especially of very small lesions, would be enhanced by a combination of high-kilovoltage techniques and spot-compression studies made during fluoroscopy. Such equipment was installed at the Grace Hospital (Main) early in the year 1956. We have since, with our technique, frequently detected polyps that were not revealed on routine high-kilovoltage studies, on double-contrast studies, or on postexpulsion studies. This technique has proved so successful in our hands that we have completely abandoned the air-contrast technique at our hospital, since the air-contrast studies failed to add any further information.

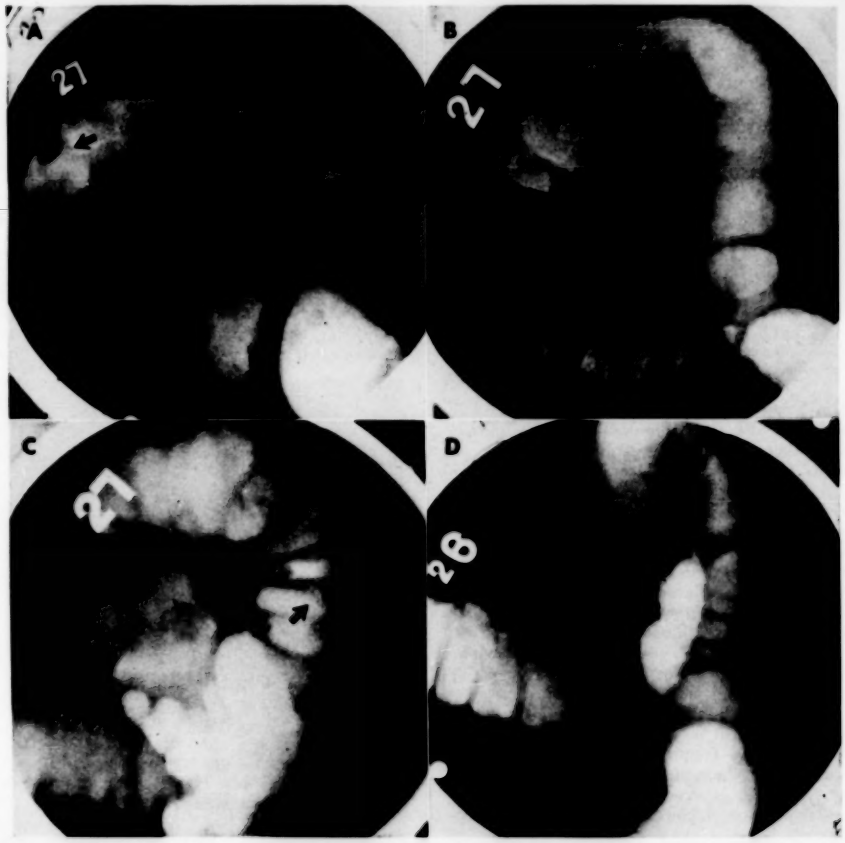

Fig. 3.—*A*, routine high-kilovoltage compression spot revealing the presence of three 8-mm. polyps in sigmoid colon in asymptomatic patient. *B*, routine high-kilovoltage compression spot revealing 7-mm. polyp in sigmoid colon. *C*, routine high-kilovoltage compression film of the splenic flexure demonstrating two unsuspected polypoid lesions not seen at fluoroscopy or on review of conventional high-kilovoltage roentgenograms. Pathological report stated adenocarcinoma. *D*, routine high-kilovoltage compression study of splenic flexure. Unsuspected small pedunculated polyp in patient with larger 1.5-cm. lesion in sigmoid (films of larger lesion not shown).

Whereas previously we had considered it a triumph to detect a colonic polyp, we were suddenly surprised to discover that lesions as small as 2 mm. in size were being detected, that multiple colonic polyps were a common finding, that polyps of the ascending colon were no longer a rarity, and that we actually had reason to believe we might approach the autopsy statistics from the standpoint of detection of such lesions (fig. 3).

Technical Factors

There are several technical factors pertinent to obtaining routine high-kilovoltage spot-compression roentgenograms. No method of examination can be reasonably effective for the detection of colonic polyps if the intestine is not well prepared. This is a fault common to all techniques, although polypoid lesions can be detected with compression techniques in the presence of fecal matter or suspected on study of the postexpulsion roentgenograms.

Our patients are prepared in the following manner if no contraindications are present clinically. 1. Liquid nonresidue diet is given during the 24 hours prior to the examination. 2. Castor oil, 1 to 2 oz. (preferably 2 oz.), is given at 6 p. m. on the day before the examination. 3. Cleansing enemas are given on the evening and morning before the examination. 4. We prefer that sigmoidoscopy not immediately precede our examination, since insufflation of air results in artifactitious defect in the barium-filled intestine which causes difficulty in the interpretation of roentgenograms.

In order to ascertain the best type of opaque medium and its proper dilution, we obtained colons from cadavers at autopsy which we filled with all types of barium and in varying dilutions. These colons were then placed in the middle of a 25-cm. masonite phantom, and x-rays were taken utilizing 120 kv. We unanimously agreed, after this experimentation and extensive clinical trial as well, on the utilization of regular barium in a dilution of 16 oz. barium (two full 8-oz. water glasses) to 3 qt. water. It is very important that the barium mixture remain in suspension throughout the study. Through extensive clinical trial we have expressed a preference for I-X barium meal. Other barium mixtures may fulfill the above requirement. This barium solution was sufficiently dense to be observed at the time of fluoroscopy and yet sufficiently penetrable to allow us to detect lesions as small as 2 mm. in size on analysis of the films. It is not necessary to use the more expensive micronized forms of barium.

We utilize a round cone measuring 6.5 in. in diameter and 2.5 in. in depth and which is mounted on a sturdy fluoroscopic screen. Smaller cones were much less effective in the sigmoid area and of practically no value when compressing the splenic and hepatic flexures of the colon. This screen is manually pressed onto the abdomen, even over the lower ribs, to flatten the colon after each segment has been optimally exposed and completely filled with barium. We routinely expose all flexures and any abnormal appearing segment at the time of fluoroscopy. After fluoroscopy, roentgenograms of the abdomen in anteroposterior and both oblique projections are exposed, utilizing high kilovoltage (120 kv.), as well as a postexpulsion roentgenogram.

Summary of Technical Data, Especially as Related to Equipment

High-kilovoltage (125-kv.) equipment tubes are used above and under the fluoroscopic table. The filtration should be increased in both tubes to 4 mm. Al. (This does not include inherent filtration.) This, of course, results in the absorption of the softer undesirable components of the x-ray beam and results in decreasing the exposure of the patient and radiologist to the x-ray. Lead equivalent or filtration in the fluoroscopic glass screen is increased to safe levels (140 kv.). Lysholm Microline stationary grid is used on the fluoroscopic screen (this is a must). It is not necessary to use a complex moving arrangement whereby Bucky exposures are made. This results only in prolonging exposure times and does not improve the technique. Electrical locking devices on the fluoroscopic screen are invaluable, since in this manner one can completely eliminate any motion of the screen during fluoroscopic exposures. Technical data suggested for fluoroscopy and high-kilovoltage spot-compression studies are given in the table.

*Suggested Technical Data for Use in Fluoroscopy and High-Kilovoltage Spot-Compression Studies**

Thickness of Patient, Cm.	Fluoroscopic Setting, Kv.	Exposure Time for Spot-Films, Sec.	Table-Top Exposure Time, Sec.
15	83	0.1	0.3
16	89	0.1	0.3
17	89	0.1	0.3
18	89	0.1	0.3
19	89	0.2	0.4
20	89	0.2	0.4
21	95	0.2	0.5
22	95	0.2	0.5
23	95	0.2	0.5
24	101	0.3	0.6
25	101	0.3	0.6
26	101	0.3	0.7
27	107	0.4	0.7
28	107	0.4	0.7
29	107	0.5	0.8
30	107	0.5	0.8

* Kilovoltage (120 kv.) and milliamperage (200 ma.) are constant for all radiographs exposed, whether spot-films or table-top exposures.

We have thoroughly investigated radiation exposure to the radiologist, according to the specifications of the Tracerlab Film Survey. For an average of over 100 fluoroscopies (45 of which were done with use of barium enemas) per week, the film survey showed exposure levels completely within accepted minimal limits over the entire body.

In an effort to determine the amount of radiation exposure which the patient received during utilization of this technique, we carried out a series of measurements utilizing the Victoreen r-meter with a masonite phantom. Our results show that the patient receives 3 r per minute to the skin surface nearest the tube at the time of fluoroscopy. The average fluoroscopic time for a patient who has been given a routine barium enema is less than two minutes and in very many instances does not exceed one minute. The area of x-ray exposure at the time of fluoroscopy on spot filming is limited to the size of the cone, which measures 6.5 in. in diameter; hence no one's skin area receives more than 1 r from fluoroscopy.

At the time of fluoroscopy three or more high-kilovoltage spot films are usually made. For a patient measuring 20 cm. in thickness across the abdomen there will be a 40-Ma.S. exposure per spot film. Utilizing 120 kv., this delivers 1 r to the skin in each area of exposure. Thus far the direct irradiation has been to skin on the patient's back. After fluoroscopy, anteroposterior and both oblique exposures of the abdomen are made utilizing 14-by-17-in. films and the overhead high-kilovoltage tube. With these exposures the patient receives 2.5 r per exposure, which is delivered to the patient's anterior abdominal wall.

Using the masonite phantom, we determined that at a depth of 5 cm. beneath the skin surface the amount of radiation was reduced by 50%. This represents a marked reduction in the amount of radiation as compared to that received by the patient who undergoes a barium enema followed by air-contrast studies. In such an examination a minimum of seven 14-by-17-in. exposures are made. Most proponents of the air-contrast technique feel that a minimum of 10 or more 14-by-17-in. exposures of the abdomen are necessary for performing a satisfactory examination. Frequently with this method repeat studies are necessary. In addition a more prolonged fluoroscopic exposure is needed when air-contrast techniques are used. Thus it is seen that in addition to the obvious advantages of detection of a larger number of polypoid lesions, we also have the advantage of reducing significantly the amount of radiation which the patient receives during such diagnostic studies.

Problems in Management Arising from Detection of Colonic Polyps in Older Asymptomatic Patients

After the institution of high-kilovoltage spot-compression techniques, the detection of very small polyps, 2 mm. to 7 mm. in size, was no longer an occasional or rare finding, nor was the detection of multiple lesions uncommon. The treatment of these patients presented a serious problem to the surgeon who was faced with the problem of localizing these lesions for conservative treatment (fulguration or polypectomy) or resorting to more radical measures (segmental resections, hemicolectomy, or complete colectomy with ileorectal anastomosis).

In our earliest experiences in which the surgeon could not locate a single small lesion, patients were not infrequently treated with segmental resection, and those with two or three small polyps in different segments of the colon were treated with hemicolectomy or total colectomy. This verified the accuracy of our findings in all cases. Fortunately at this time studies carried out by Drs. Arminski and McLean [5] of our staff, based on the analysis of 673 consecutive polyps, revealed that the incidence of malignancy in polyps 5 mm. or less in size was less than 0.2% and that the incidence of malignancy in polyps 1 cm. or less in size was less than 2%.

On reviewing Hultborn's [6] monograph dealing with cancer of the colon and rectum, and especially the section dealing with autopsy data relating the incidence of colonic polyps, correlation of incidence with age, and their neoplastic potential, we were impressed with two circumstances. First, in the older age group, 60 and over, at least 50% of people had one or more polyps at autopsy. Second, the cancer potential, always admittedly present, was actually very low, especially in the smaller lesions. A common misconception is that most polyps are found in the rectosigmoid area, whereas Hultborn's data as well as a statistical analysis of autopsy cases by Drs. Arminski and McLean at our hospital shows an equal distribution of polyps throughout the colon.

Since the incidence of malignancy in polypoid lesions varies from 0.2% to 50%, it is obvious that more clear-cut histopathological criteria must be established for the evaluation of these lesions, since with our method the frequency of detection of such lesions could parallel the autopsy findings, especially as it relates to lesions 2 mm. in size and larger. According to multiple autopsy surveys, the incidence of polyps in patients over 60 years of age is 50%. Is every other patient to have his intestine explored or partially removed?

In view of these considerations we suggest that surgery is not necessarily indicated in the older asymptomatic patient with polyps 5 to 7 mm. in size or less, or even if multiple small polyps are present, especially if these small lesions are localized in different segments of the colon, thus complicating the problem of treatment. Forty per cent of the patients may have multiple lesions, and the cancer potential in any given polyp is the same. We have been able with this technique to demonstrate polyps and polypoid lesions with such clarity that size and shape can be accurately and repeatedly recorded in most instances. We propose that it is a safe and simple procedure to observe these small lesions at periodic intervals for change in size. If growth occurs or symptoms (bleeding) develop, removal can be considered.

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We are currently following a large number of such cases at six-month intervals, none of which, to date, have shown any change. Some of these cases have been followed as long as 18 months. We hope in this manner to acquire a more clear-cut understanding of the cancer potential of these lesions and in this manner to establish more definitive concepts and criteria for their management.

Summary

The current concept that polypoid lesions of the colon are potentially malignant necessitates the use of a simple, accurate, routine method for their detection whether the patient is symptomatic or asymptomatic. Most radiologists still rely on the double-contrast enema for the detection of such lesions; however, they openly admit the inadequacy of this method, especially as a routine procedure.

We have evaluated all known techniques and have decided that the simplest and most accurate method available combines the use of large-field spot-compression roentgenograms in the high-kilovoltage range with a highly filtrated beam. We have been successful in detecting lesions as small as 2 mm. in size by this method. In a majority of these cases other accepted techniques (high-kilovoltage and double-contrast) were unsuccessful in the detection of these small lesions as well as occasional larger lesions.

The problem arising from this approach is no longer one of detection but rather the management of these lesions. It is also imperative that clear-cut histopathological criteria be established in order that there be some uniformity of opinion regarding the evaluation of such lesions. Future management of smaller asymptomatic lesions not accessible to treatment by endoscopy will be in great deal dependent upon the results of such an evaluation.

It is our opinion currently that the smaller asymptomatic lesion beyond the reach of the sigmoidoscope in the older patient can be followed conservatively; we have followed many patients at six-month intervals, none of which have shown any change. It is our intention to continue follow-up in such cases until a more definite understanding of the neoplastic potentiality is established.

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ALLERGIC REACTIONS TO DRUGS.—Allergic reactions to drugs may have consequences which are out of all proportion to the conditions for which many drugs are given. Because of this, every attempt should be made to eliminate needless administration of drugs and, when possible, to give them under conditions which appear to be least conducive to the development of allergy. Accordingly, it will probably be in the best interest of the patient to prescribe the fewest number of drugs compatible with effective treatment, to give drugs orally when possible rather than by injection, to question the patient first as to the past occurrence of untoward reactions to drugs and to avoid the topical administration of those drugs which are effective and safe when given by mouth or by injection. In those instances wherein there is the possibility that the patient may already be allergic, a short-acting, rather than a long-acting preparation should be given.—F. C. Lowell, M.D., Allergic Reactions to Drugs, *The Practitioner*, June, 1957.

GLAUCOMA IN MEDICAL PRACTICE

DANGER OF USE OF SYSTEMIC ANTISPASMODIC DRUGS IN PATIENTS PREDISPOSED TO OR HAVING GLAUCOMA

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Drugs given for their antispasmodic, sympathomimetic, or parasympatholytic effects in gastrointestinal disease and other systemic conditions generally have important incidental effects upon the eye. Mydriasis and cycloplegia can raise the intraocular pressure and precipitate acute attacks of glaucoma in some cases. But this association of effects is not inevitable, and dicyclomine is an example of drugs that are effective as antispasmodics without exerting dangerous side-effects on the eye. This is illustrated in a study of pupil sizes and intraocular pressures in 53 subjects with normal intraocular pressures and 17 patients with chronic simple glaucoma; the well-known cycloplegic effect and ability to increase intraocular pressure was demonstrated for atropine and related drugs, as was the absence of these dangerous effects when dicyclomine was given in antispasmodic doses to patients with chronic simple glaucoma. Physicians who prescribe atropine or similar drugs for the relief of gastrointestinal disease and Parkinsonism should be acutely aware of the disastrous effects these drugs may have on the eyes of patients who have glaucoma or are predisposed to it. They should also be aware of the existence of antispasmodics relatively free from these effects.

Glaucoma is the name applied to a symptom complex of a progressive loss of the visual field due to an increase in the intraocular tension which may or may not be accompanied by pain. One type, chronic simple glaucoma, is one of the most important causes of blindness among adults. The onset of this type is usually insidious with little ocular discomfort or pain and therefore ignored by the victim until irreparable damage to the eye and vision results, unless the diagnosis is made by a physician and early treatment instituted.

In another type, acute glaucoma, there is an acute rise in intraocular tension accompanied by severe pain which cannot be ignored by the patient and which requires immediate lowering of ocular tension if blindness is to be prevented. The accepted cause for this sudden rise in ocular tension (in acute glaucoma) is a dilatation of the pupil, which

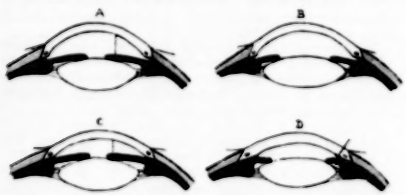

Fig. 1.—*A*, diagrammatic cross section of eye with normal depth of anterior chamber; *B*, dilatation of iris in eye with normal anterior chamber; *C*, cross section of eye with shallow anterior chamber; and *D*, dilatation of eye with shallow anterior chamber causes folds in iris resulting in blockage of angle of filtration.

occurs in eyes with shallow anterior chambers, crowding the iris into the anterior chamber angle and obstructing the outflow of fluid from the eye (fig. 1). If the dilatation is marked and persistent, the typical attack of acute glaucoma ensues in those eyes which are predisposed to glaucoma. Frequently, when the dilatation is only moderate, a slight increase in intraocular pressure may occur and then resolve.

The dilatation of the pupil by atropine, scopolamine (Hyoscine) hydrobromide, belladonna or belladonna-like drugs taken orally causes relatively little change in the intraocular tension in the normal eye. However, in certain eyes with chronic glaucoma, or in eyes with a predisposition to glaucoma, certain systemic antispasmodic medicaments may produce a dangerous increase in the intraocular tension, which may result in an acute attack of glaucoma.

Blurred vision is a common complaint of patients using sympathetic antispasmodic drugs. This is due to the paralyzing effect on the ciliary muscles and the consequent loss of accommodation. The sphincter of the iris is likewise affected, thus causing a dilatation of the pupils. Occasionally the dosage of belladonna or its derivatives has been prescribed by the medical practitioner who utilizes this symptom of blurred vision as an indication of the point at which the drug will relieve muscle spasms of the gastrointestinal tract (i. e., "take this medicament until the vision is blurred"). Therefore, it should be clearly understood that an acute attack of glaucoma may be induced by the oral administration

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of these drugs in this way and that, in some instances, they may even nullify the effect of miotic drugs being instilled in glaucomatous eyes.

At the glaucoma clinic of the New York Eye and Ear Infirmary, a number of patients with chronic glaucoma did not respond to treatment with miotics after varying periods of adequate control. All were found to be taking certain systemic antispasmodic drugs for various systemic conditions such as gastrointestinal disorders, duodenal and gastric ulcers, and Parkinsonism. The increased tension was eventually controlled by the use of standard miotics in these patients after the antispasmodic medication had been discontinued.

A survey of the literature showed that Hufford [1] treated two patients who were suffering from glaucoma and the irritable colon syndrome with dicyclomine (Bentyl) hydrochloride, given orally, without effecting an increase in the intraocular tension. Brown and Guilbert [2] reported a case history of a male who developed glaucoma after being treated for peptic ulcer with tincture of belladonna. Dicyclomine was substituted for the belladonna, and as a result the intraocular tension was normal throughout the one-month period of treatment with this drug. Dicyclomine is a synthetic agent with parasympatholytic action on the gastrointestinal tract.

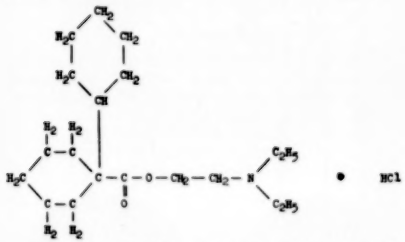

Fig. 2.—Structure of dicyclomine (Bentyl) hydrochloride.

Pharmacological studies [3] indicated that smooth muscle spasm could be relieved without side-effects, notably mydriasis. This was confirmed by comparative studies with adiphenine (Trasentine) hydrochloride and papaverine hydrochloride against the stimulation produced by acetylcholine which is ⅛ that produced by atropine, while the mydriatic action is only 1/400 that of atropine.

In order to evaluate further the effect of the ingestion of various antispasmodic drugs upon the pupil size, amplitude of accommodation, and ocular tension, a study was instituted at the New York Eye and Ear Infirmary in patients with normal intraocular tension and in patients with chronic simple glaucoma. A Schiøtz tonometer was used to measure the intraocular pressure of the eyes of all the subjects participating in the study; the size of the pupil was measured with a pupillometer, and the amplitude of accommodation was observed before, during, and after the oral administration of (1) placebos, (2) belladonna and belladonna-like drugs, and (3) dicyclomine. The subjects were observed for a period of from one to six days, and the maximum findings in each case were recorded.

TABLE 1.—*Effects of Placebos on Ocular Function in Eight Patients with Normal Tension*

Patients, No.	Changes in*	
	Pupil Size, Mm.	Ocular Tension (Schiøtz), Mm. Hg
2	−1.0	0.0
1	−2.0	0.0
1	−1.5	−2.0
1	0.0	0.0
1	0.0	−1.0
1	+0.1	+1.0
1	+0.3	+1.0

* There were no changes in accommodation.

The effects of placebos on the ocular function in eight patients with normal intraocular tension are shown in table 1. There was no change in the accommodation in any of the eight patients to whom placebo had been administered. In two eyes, there was no change in the pupil size, and in the third and fourth cases, the size difference was considered insignificant (+0.1 and +0.3). The pupillary size decreased 1 mm. in two eyes, 1.5 mm. in one, and 2 mm. in one. Intraocular tension remained unchanged in four eyes (50%), increased 1 mm. Hg (Schiøtz) in two, decreased 1 mm. Hg in one, and decreased 2 mm. Hg in one.

The effects of belladonna and belladonna-like drugs in the ocular functions in eight patients with normal ocular tension is shown in table 2. The use of these preparations resulted in no change in the accommodation of 50% of the eyes with normal ocular tension and a slight to moderate decrease (paresis) of accommodation in 50%. The slight increase in the pupil size of the eyes in these eight cases is relatively insignificant. In only one eye was the intraocular tension unchanged. An increase of 1 mm. Hg (Schiøtz) was noted in two eyes, an increase of 2 mm. Hg in two, and an increase of 3 mm. Hg (Schiøtz) in three.

TABLE 2.—*Effects of Belladonna and Belladonna-like Drugs in Eight Patients with Normal Ocular Tension*

Case No.	Drug	Dosage*	Length of Therapy, Days	Changes in		
				Accommodation (Near-Point Convergence)	Pupil Size, Mm.	Ocular Tension (Schiøtz), Mm. Hg
1	Antispasmodic	50 mg.	2	Increase	+0.3	+2
2	Antispasmodic	50 mg.	1	None	+0.4	+3
3	Antispasmodic	50 mg.	1	Moderate decrease	+0.1	+1
4	Benethine	50 mg.	1	None	+0.2	0
5	Benethine	50 mg.	1	None	+0.1	+1
6	Belladonna	6 drops	...	Slight decrease	+0.6	+3
7	Belladonna	6 drops	...	Moderate decrease	+0.3	+3
8	Belladonna	6 drops	...	None	+0.4	+2

* Three times daily.

The effects of various dosages of dicyclomine on the ocular function in 37 patients with normal ocular tension is shown in table 3. Only 3 of the 37 persons with normal ocular tension and who used dicyclomine had slight decreases in the accommodation. The slight increase in the size of the pupil in 12 eyes is insignificant. There was no change in the intraocular tension in 20 eyes, and in the remaining 17 there was a decrease in intraocular tension from 1 to 6 mm. Hg (Schiøtz).

TABLE 3.—*Effects of Dicyclomine Hydrochloride on Ocular Function in Thirty-Seven Patients with Normal Ocular Tension*

	Dicyclomine		Changes in		
Patients, No.	Dosage, Mg.	Doses, No.	Accommodation	Pupil Size, Mm.	Ocular Tension (Schiøtz), Mm. Hg
2	10	1	None	0.0	0
1	10	1	Slight decrease	0.0	−6
1	10	1	None	0.0	−4
1	10	1	None	+0.3	0
1	10	1	None	0.0	−3
1	10	1	None	+0.3	−1
1	10	1	None	+0.5	−3
1	10	1	None	0.0	−2
2	20	1	None	+0.1	0
2	20	1	None	0.0	0
1	20	1	None	+0.3	−2
1	20	1	None	+0.3	−1
1	20	1	None	0.0	−2
8	20	9*	None	0.0	−2
3	20	9*	None	0.0	0
1	20	9*	Slight decrease, 2nd and 3rd days	+0.1	−2
1	20	9*	Slight decrease, 3rd day	+0.3	−2
4	20	1	None	0.0	0
1	30	1	None	0.0	−1
1	30	1	None	0.0	−3
1	30	1	None	+0.1	−1
1	30	1	None	+0.5	−2
1	30	1	None	+0.2	0
1	30	1	None	+0.4	0

* One dose three times daily for three days.

TABLE 4.—*Effect of Dicyclomine Hydrochloride on Ocular Function in Seventeen Patients with Chronic Simple Glaucoma*

			Changes in*	
Case No.	Dicyclomine Dosage, Mg.†	Length of Therapy, Days	Pupil Size, Mm.	Ocular Tension (Schiøtz), Mm. Hg
1	10	3	0.0	0
2	10	‡	0.0	0
3	10	‡	0.0	−4
4	10	‡	0.0	−2
5	10	1	0.0	−3
6	10	7	0.0	0
7	10	7	0.0	−3
8	10	4	0.0	+1
9	10	2	0.0	+1
10	10	6	0.0	0
11	20	3	−0.2	0
12	20	5	−0.1	0
13	20	3	−0.2	0
14	20	3	0.0	−2
15	20	4	−0.2	0
16	20	10	−0.2	+1
17	40	6	−0.1	+1

* There were no changes in accommodation.
† Three times daily.
‡ One dose only.

The effects of varying doses of dicyclomine on the ocular function in 17 patients with chronic simple glaucoma are shown in table 4. The oral administration of varying doses of dicyclomine had no effect on the accommodation of 17 patients with chronic simple glaucoma. There was no change in pupillary size in 11 eyes, and the minor decrease in the size of the pupil in the six was insignificant.

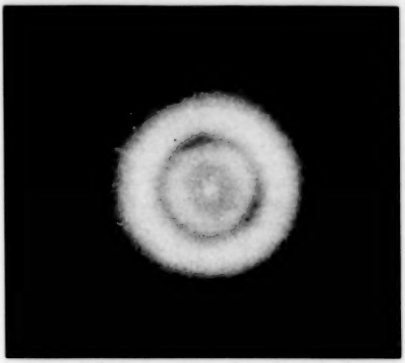

Fig. 3.—Subjective symptom of patient with glaucoma. Multicolored partial or complete rings (halos) around bared light bulb.

There was no change in ocular tension in eight eyes, a decrease from 3 to 4 mm. Hg (Schiøtz) in five, and an increase of 1 mm. Hg in four.

Comment

From the data presented on the effects of various antispasmodic drugs taken orally, it is believed that the medical practitioner should not only exercise extreme caution in prescribing any systemic drugs but should also be fully aware of some of the ocular signs and symptoms in eyes predisposed to glaucoma and those with glaucoma in the early stages.[4] Three steps should be taken by the physician.

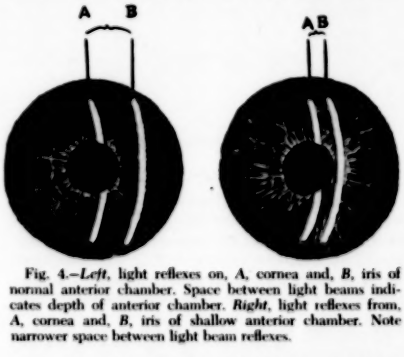

Fig. 4.—*Left*, light reflexes on, *A*, cornea and, *B*, iris of normal anterior chamber. Space between light beams indicates depth of anterior chamber. *Right*, light reflexes from, *A*, cornea and, *B*, iris of shallow anterior chamber. Note narrower space between light beam reflexes.

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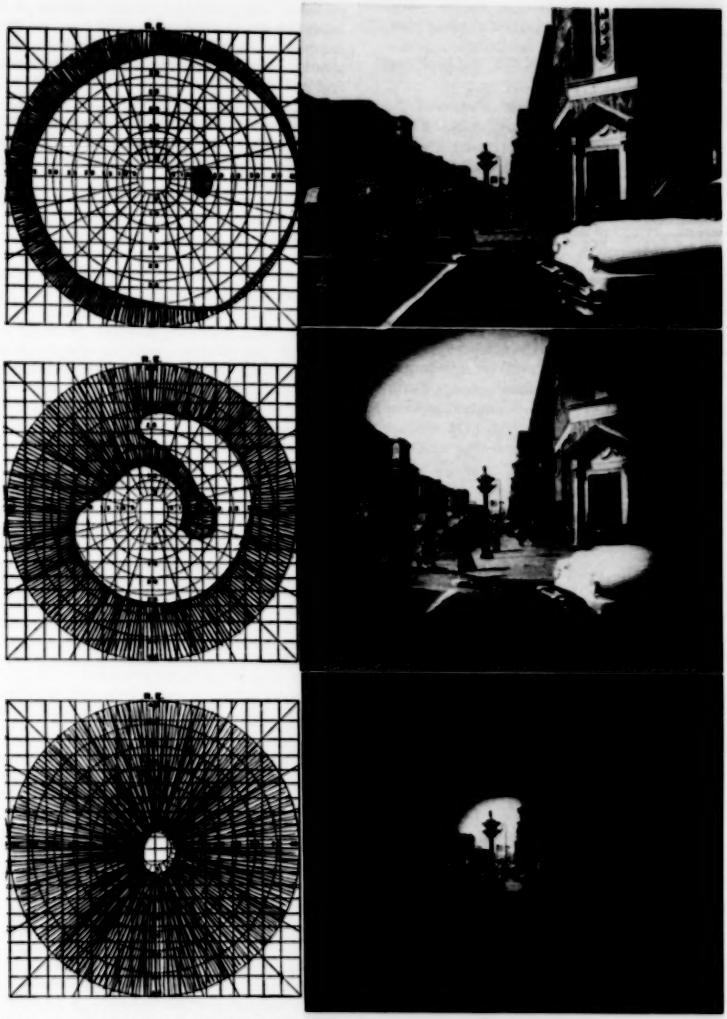

Fig. 5.—*A*, normal visual field of healthy eye encompasses panorama; *B*, beginning contraction of visual field blocks out some peripheral vision; and *C*, advanced glaucomatous contraction of visual field and decreased peripheral vision.

1. The history should be carefully investigated for the presence of diagnosed glaucoma or a family history of this condition. Recent studies [5] have revealed a high familial incidence of chronic glaucoma as well as the presence of shallow anterior chambers in a large percentage of children and siblings of parents with acute glaucoma.

2. An evaluation should be made of some of the subjective complaints related to glaucoma. These include attacks of blurred vision (intermittent or constant), partial or complete halos seen around a bared electric light bulb (fig. 3), complaints of pain in the eyeball or around the eyes, difficulty with the field of vision (described by the patient as defective "side vision"), and discomfort with close work even with corrective glasses.

3. An observation of the patient should be made for the presence of the following diagnostic (objective) symptoms: *a.* The presence of a dilated pupil which reacts sluggishly or not at all, especially when associated with a "muddy" appearance of the iris. *b.* An extremely shallow anterior chamber. This may be determined by shining a streak light which forms narrow beams of light reflexes from the corneal and iris surfaces on the eye. The space between the light beams indicates the actual depth of the anterior chamber (fig. 4). *c.* Constriction of the visual field, beginning on the nasal side and gradually involving the temporal field of vision until a "tubular" visual field results (fig. 5). The confrontation test is a rapid preliminary test for comparing the patient's field of vision with that of the examiner. A light should be adjusted to about one foot above the patient's head. The patient and examiner should be seated one meter apart, directly facing each other, and with eyes on the same level. The examiner closes his right eye; the patient covers his left eye and fixes the examiner's left eye with his right. Midway between the examiner and patient, a 3-mm. white-headed pin is carried toward the center (from above and below, nasally and temporally, and then along meridians between these points). If visual acuity is low, a finger which is wiggled, or a hand, may have to be used as a test object. The patient should be requested to indicate when the object becomes visible. In this way the limits of the field of vision of the patient's right eye are compared with those of the examiner's left eye. In the same manner the limits of the field of the patient's left eye should be compared with those of the examiner's right eye. *d.* Increased intraocular pressure. This may be determined with a standard tonometer or an ocular hypertension indicator.[6] Patients exhibiting any of these signs or symptoms should be referred to an ophthalmologist.

Summary

Physicians should take care in prescribing certain systemic antispasmodic drugs, because of the inherent danger of glaucoma. The common signs and symptoms in patients predisposed to glaucoma should be watched for. In our study belladonna and belladonna-like drugs, taken orally, produced a mild increase in the intraocular pressure in eight patients with normal tension. The size of the pupil and the accommodation was also affected in 50% of these patients. The effects of dicyclomine (Bentyl) hydrochloride in 37 patients with normal tension and in 17 patients with chronic simple glaucoma indicates that dicyclomine does not significantly increase the intraocular pressure, nor does it affect pupil size or accommodation of the eye. This medicament appears to be somewhat safer than other antispasmodic drugs tested in patients who are predisposed to or have glaucoma. Medical practitioners who prescribe atropine or its derivatives, as well as certain synthetic parasympatholytic agents, for the relief of various gastrointestinal disorders and Parkinsonism should be acutely aware of the disastrous effect that these antispasmodic drugs may have on the eyes of patients with either a predisposition to glaucoma or diagnosed glaucoma.

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FECAL INCONTINENCE—NONSURGICAL TREATMENT

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In the treatment of fecal incontinence, nonsurgical measures are often as important as the surgical, and in patients whose incontinence is neurogenic, as in paraplegia, only nonsurgical therapy can help. Nonsurgical measures for fecal incontinence fall into five phases: diet, drugs, irrigations, exercises for the anal muscles, and psychotherapy. Continence is maintained not so much by tonically contracted states of the internal or external sphincters of the anus as by reflex contractions of the external sphincter initiated in the rectum. An additional neuromuscular mechanism described as reservoir continence resides in the descending colon. Fecal incontinence is frequently the unfortunate price that has to be paid for lifesaving surgery, and at least half of the patients who complain of varying degrees of fecal incontinence date its onset to some surgical procedure. It is essential for their rehabilitation that they be instructed in the use of the nonsurgical measures here described.

The inability to restrain natural bodily discharges, although not a menace to life, is a great handicap to those so afflicted, often creating mental anxiety and semi-invalidism. Some persons with incompetence of the anorectal musculature that causes leakage, soiling, or fecal incontinence can be helped by surgical intervention, but it is necessary to select with care those who might be amenable to such management. At best, surgical treatment has its limitations, and its results frequently fall short of restoring the patient to normalcy. Nonsurgical procedures may be of great benefit to patients who cannot be helped surgically or who continue to have some difficulty after an operation to restore continence. Before such measures are discussed, it is important to understand the factors that enter into the maintenance of intestinal continence.

Mechanism of Intestinal Continence

Muscular Factors.—In the past, fecal continence was credited to the external sphincter or puborectalis muscle or both. The old idea that the internal sphincter plays an important role in maintaining fecal continence has been largely disproved by Denny-Brown and Robertson,[1] as well as by Gaston,[2] who demonstrated that this muscle relaxes as the rectum contracts and probably expedites defecation. Gaston [2] also pointed out that it is a fallacy to assume that tonic sustained contraction of the external sphincter maintains continence for longer than a minute or so, except perhaps in periods of stress. It is impossible to maintain prolonged contraction of this muscle.

Anal musculature may overlie a fistulous tract. Division of such musculature, as is frequently done during fistulotomy, usually does not affect voluntary control except for perhaps the first few weeks after operation. On the other hand, temporizing or long delays in beginning surgical treatment of anal fistulas may lead to anal incontinence or at least incompetence of the muscles, because the associated long-standing infection and recurring abscesses have created so much fibrosis that the voluntary muscles are immobilized by it. This is particularly true in chronic ulcerative colitis complicated by anal fistula.

Neuromuscular Factors.—Gaston [3] described two mechanisms that maintain anal and intestinal continence, namely (1) a reflex involving the rectum and external anal sphincter and (2) a reservoir continence in the descending colon. Although the external anal sphincter is usually relaxed, peristaltic pressure in the rectum causes this muscle to contract reflexly in a few seconds; this contraction persists until the reflex peristaltic pressure ceases. As just noted, this reflex is initiated in the rectum and not in the anal canal. Many patients who have had the rectum removed and the anal sphincters preserved, as in certain types of "pull-through" procedures for removal of carcinoma of the rectum, have variable degrees of fecal incontinence. The preserved anal muscles can be contracted voluntarily, and, from an objective standpoint, these patients should have perfect control. However, because the reflex mechanism is destroyed when the rectum is removed, the patient does not know when to contract his preserved anal muscles. Furthermore, he has difficulty in differentiating between flatus, liquid stool, and formed stool, and soiling is the result. Gaston [3] considered that the afferent impulse of the reflex is maintained only when the distal fourth of the rectum is preserved.

The second neuromuscular mechanism, called "bowel or reservoir continence," is said to reside in all parts of the descending colon. The descending colon acts as a reservoir independent of sphincteric action, which explains why some patients with a scarred, deformed anus who are unable to demonstrate any voluntary action of the anal muscles and

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who from an objective standpoint would appear to have complete anorectal incontinence experience little or no soiling or leakage of intestinal contents. It also explains why some abdominal colonic stomas on the left are easily managed and why some patients with such stomas apparently obtain a fair degree of control of intestinal evacuation.

On the other hand, patients who have erratic bowel habits, such as in the irritable-colon syndrome, with its episodes of constipation, diarrhea, and excessive production of mucus, or those who have organic colonic disease, such as chronic ulcerative colitis, have little or no reservoir continence. Such a patient with a scarred, deformed anus and inefficient anal muscles is likely to have great trouble with control of intestinal contents. If one is to do certain anorectal surgical procedures on such patients with an absent reservoir continence, some degree of leakage or soiling can be anticipated in numerous instances.

Causes of Anal Incontinence

The causes of anal incontinence are many, and the degree varies greatly. A satisfactory classification includes three main types, namely (1) traumatic, (2) congenital, and (3) acquired (nontraumatic).

Traumatic Causes.—At least half of all instances of traumatic anal incontinence have their onset after some anorectal surgical procedure. The number of patients who have incontinence after anorectal fistulectomy or fistulotomy is decreasing, owing principally to the fact that long-continued postoperative packing of the wound is no longer in vogue. Leakage of mucus or stool or inability to retain gas is not uncommon after radical hemorrhoidectomy or local excision in cases of prolapse of the rectal mucosa. This difficulty is caused principally by the presence of scar tissue, which makes the anal musculature less efficient. Most of these patients with postoperative incontinence have poor reservoir continence. Postoperative difficulty with bowel control in many patients of this group, which is common after removal of the rectum with sphincteric preservation, is the unfortunate sequence of a lifesaving procedure. Most of these patients would be happier with an abdominal colonic stoma.

Other traumatic causes of incontinence are lacerations from falls in which the anorectum may be impaled and lacerated, or injuries to the head or spinal cord resulting from automobile accidents. Third-degree perineal lacerations resulting from childbirth and causing incontinence are being seen less frequently, owing to better maternal care at the time of delivery. Some patients date the onset of incontinence to the induction of spinal or caudal anesthesia or to an injection of alcohol for pruritus ani. Most patients with traumatic incontinence can be helped by a systematic plan of nonsurgical measures.

Congenital Causes.—Anal incontinence may be associated with megacolon or congenital malformations of the anorectum, such as an imperforate anus with perineal, vaginal, or scrotal fistulas. Surgical correction of such defects is indicated, but such treatment frequently must be followed or supplemented by nonsurgical measures.

Acquired (Nontraumatic) Causes.—An increasing proportion of people are in the older age groups. Many of these older persons have variable degrees of hemorrhoids, mucosal prolapse, poor muscular tone, or dulled reflexes. Therefore, senility now is a common cause of some degree of incontinence. Fecal impaction in the lower portion of the intestine may cause partial obstruction and diarrhea, and in such instances the patient is unable to restrain the intestinal contents. Impaction is relatively common in elderly persons and in mentally ill patients. Inflammatory processes that have infiltrated the rectal walls, such as in extensive internal fistulas and the stricture of lymphogranuloma venereum, immobilize the musculature, destroy the anorectal reflexes, and result in variable degrees of incontinence. Malignant tumors and strictures of the rectum, especially if they are low in the rectum and have infiltrated the rectal walls, likewise inhibit the normal reflexes and cause partial obstruction, with constipation and diarrhea and secondary incontinence. Patients with rectal prolapse usually have some degree of incompetence of the anal muscles because of the poor muscular tone. If these patients have good reservoir continence, the inadequacy of the anal muscles is usually more obvious objectively than it is subjectively. Even after the prolapsed rectum has been treated surgically, some degree of fecal incontinence may persist, requiring nonsurgical measures.

Selection of Patients for Treatment

Although it is not within the scope of this paper to deal with the surgical management of anorectal incontinence, it is important to determine which persons may be helped by surgical treatment, by a combination of surgical and medical management, or by nonsurgical methods alone. When a scarred deformity of the anus exists, such as a deep scarred sulcus that is the aftermath of fistulectomy or fistulotomy, the most that the surgeon can accomplish is to excise the scarred defect and to suture the denuded surfaces together. It does not necessarily follow, however, that complete continence will be restored, and it is likely that such a patient will continue to have some difficulty, especially if an irritable colon and a diminished reservoir continence are present. Approximation of the severed ends of the anal muscles may look well in schematic diagrams, but in actual surgical practices the procedure amounts to getting rid of a block of scar tissue which acts as a mechanical impediment to the effi-

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ciency of the muscles. Technical difficulty arises at the time of operation because the ends of the muscle are bound down in scar tissue, atrophied, and retracted, and frequently it is difficult or impossible to identify them.

Patients who have third-degree perineal lacerations resulting from childbirth or who have congenital anomalies usually are benefited by appropriate surgical treatment, but this frequently must be supplemented by nonsurgical procedures. Patients, such as elderly persons with poor muscular tone, who have acquired, nontraumatic incontinence are those most benefited by nonsurgical measures, as are those who have had removal of the rectum with preservation of the sphincter. Patients who have neurogenic incontinence resulting from interruption of the nerve supply to the perineum, rectum, and bladder, as in paraplegia, spina bifida, or meningocele, would not be candidates for any anorectal surgical procedure, but such patients can be helped by nonsurgical therapy.

Nonsurgical Measures for Rectal Incontinence

Nonsurgical measures for rectal incontinence fall into five phases, namely (1) diet, (2) drugs, (3) irrigation of the lower part of the intestine, (4) exercise for the anal muscles, and (5) psychotherapy. These forms of treatment can be used singly or in combination, as the patient's particular problem dictates.

Diet.—The diet is of a low-residue type and should be as simple as possible for the patient to follow. A convenient method of instructing these patients is to give them a list of foods that may be included in the diet and a list to be excluded. Most patients know what foods or liquids tend to produce loose stools, and these, of course, are placed in the restricted list. The patient's intake of fluids should be limited. A sample of a minimum-residue diet is shown in the table. Complete vitamin supplementation is necessary for patients on such a dietary regimen.

Drug Therapy.—Drug therapy includes use of drugs that decrease intestinal peristalsis and those that tend to "soak up" water from the intestines, thus giving more form to the stool. Many satisfactory preparations will help to reduce intestinal motility. Belladenal tablets, containing ¾ grain (50 mg.) of phenobarbital combined with 1/250 grain (0.25 mg.) of the alkaloids of belladonna, have been satisfactory. Usually, half of such a tablet before each meal is an adequate dose. Preparations such as this are particularly indicated in patients who have the irritable-colon syndrome or when emotional upsets precipitate a bout of diarrhea. Other anticholinergic drugs of proved value are methantheline (Banthine) bromide, 50 mg. after each meal, or propantheline (Pro-Banthine) bromide, 15 mg. after each meal.

It might appear inconsistent to administer the so-called bulk preparations, or hydrophilous agents, to a patient on a minimum-residue diet, but such preparations as methylcellulose, given as 0.5-Gm. tablets, do have a facility for "soaking up" water and producing more form to the stool. The doses must be individualized, but administration of 3 to 6 tablets after each meal, with a limited intake of fluids, is usually of value. Various preparations of karaya are effective in a similar manner. Many patients with traumatic anal incontinence associated with episodes of diarrhea of a functional nature respond well to drug therapy.

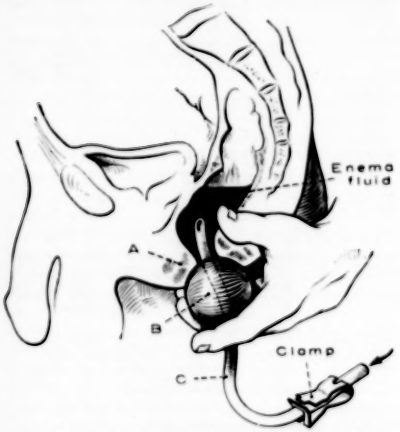
Intestinal Irrigation.—The aforementioned measures of diet and drugs frequently are combined with irrigation of the lower part of the intestine when seepage or leakage throughout the day is a problem. After the initial bowel movement of the day, the patient is instructed to "wash out" the lower reaches of the intestine with a plain enema of warm water. He is advised to fasten a hook on the bathroom wall on which the enema can or bag may be hung. Instead of the ordinary enema tip, an 18 F. to 26 F. catheter is used because it can be inserted higher into the rectum and trauma is less likely to occur from its frequent use. Many patients will state that they have difficulty retaining the water, but the mere exercise of trying to hold the water is beneficial. When a large anal defect is present and retention of water is mechanically impossible, a Bardex-Foley type of rectal bag and catheter may be used instead of the regular catheter. The patient

Foods Included and Excluded in a Minimum-Residue Diet

Type of Food	Foods Included	Foods Excluded
Beverage	Carbonated beverage; cereal beverage; coffee; tea	Milk, milk drinks
Bread	White or fine rye bread, toasted, with emphasis on enriched types; saltines; soda crackers; rusk	Bread or crackers containing whole-grain flour or bran; quick breads
Cereal	Cooked refined corn, rice, and wheat cereal; strained oatmeal; commercially prepared cereals from corn or rice free from outer coating	Whole-grain cereals
Dessert	Cakes; cookies; custards; gelatin desserts; ice cream; puddings; rennet desserts; sherbets; all without fruit or nuts	Any other
Fat	Butter; cream; fortified margarine	None
Fruit	Strained fruit juice, including 1 citrus-fruit juice daily	Any other
Meat, egg, cheese	Bacon, tender meat, fish and fowl except those listed under "Foods Excluded"; canned fish; eggs, cottage or cream cheese; cheddar (American) cheese used only as flavoring in cooking	Fried meat, fish or fowl; fresh pork; cheese other than listed under "Foods Included"
Potato or substitute	Macaroni; noodles; refined rice; spaghetti	Potato; hominy; whole-grain rice
Soup	Bouillon; broth	Any other
Sweets	Candy except that listed under "Foods Excluded"; honey; jelly; molasses; sirups; sugar	Candy containing fruit or nuts; jam; marmalade
Vegetable	Tomato juice	Any other
Miscellaneous	Gravy; herbs except garlic; salt; spices; vinegar; white sauce	Garlic; nuts; olives; pickles; popcorn; relishes

is shown how to press the distended Bardex bag against the perineum to close the anal defect so that the water can be retained.

For several years, my colleagues in roentgenology have used an effective means of having the incontinent patient retain barium during roentgenologic studies on the colon. A hole is drilled through the center of an inexpensive, soft-rubber ball about the size of a tennis ball, which may be purchased at most any dime store; the bore of this hole is slightly smaller than the caliber of the catheter to be used. The catheter is then pulled or pushed through the hole in the ball. If the rubber catheter is stretched slightly, its diameter is decreased sufficiently so that it may be easily pushed through the slightly smaller bore in the ball. Thus, when the stretch is released, the catheter is well anchored in place. It is used in a manner similar to that of the



Mechanical method of retaining fluid in irrigation of lower part of intestine in patient with defective anus. *A*, incompetent anus. *B*, rubber ball pressed against the perineum acts as dam to assist in retaining fluid. *C*, catheter threaded through ball.

Bardex bag to produce pressure on the defect so that water can be retained (see figure). This simple equipment has been extremely valuable for many patients with anal deformities and defects who have difficulty retaining enemas. If much stool is expelled with the first irrigation or enema, the patient is advised to repeat it a second or even a third time. Since many of these patients are elderly, their first attempt at the procedure should be under the supervision of a nurse or physician.

The irrigation accomplishes two purposes. First, it rids the lower intestine of stool, so that the patient is less likely to have leakage. In the second place, most of these patients have a variable amount of scar tissue in the anorectal region that tends to immobilize the muscle and make it less efficient. The warm irrigating fluid aids in making this scar tissue more resilient, and the mere practice of trying to retain the warm water will help to strengthen the muscles in that region.

Muscle Exercises.—A systematic plan of exercising the voluntary anal muscles appears to be of some value in elderly patients or in those who have some degree of incontinence after radical hemorrhoidectomy or fistulectomy, when inability to retain gas or seepage is a problem and when muscle is present but weak or inefficient. The patient is instructed to do the exercises three times daily for five minutes while lying down. The external sphincter is contracted and held in this state while the patient counts slowly to five; then the muscle is relaxed and the contraction is repeated. The contraction should be vigorous and sustained for about five seconds. Many patients apparently do not know how to contract the sphincter even though they may have the ability to do so. It is best to have the patient demonstrate this contraction while on the proctoscopic examining table. These exercises are continued for two or three months. Combining these exercises with warm-water irrigation of the lower part of the intestine is a definite help to many patients.

Psychotherapy.—Patients vary greatly in their psychic attitude toward incontinence. Of two persons with the same degree of anal incontinence, one may ostracize himself completely from society, while the other is little, if any, concerned about the incontinence. Similar variations in reaction occur in women who have rectovaginal fistulas. Daniels [4] found that about 25% of women who had such fistulas and who pass gas and sometimes stool by way of the vagina did not consider it enough of a problem to accept surgical intervention. Likewise, the elderly woman with an extensive third-degree perineal laceration of 30 or more years' duration frequently declines surgical treatment, accepting her incontinence as a natural consequence of childbearing. As in any other psychotherapeutic procedure, a careful analysis of the problem is necessary in order to make reassurance effective. Many of these patients have gotten into the habit of wearing a diaper, which is unsound psychologically. It is well for the patient to dispose of this habit after the measures of diet, drugs, irrigations, and exercises already described are started in order to help restore confidence.

Summary

Although surgical treatment has a place in helping the patient with fecal incontinence, its results frequently are not entirely satisfactory. This is particularly true in patients who have absent or poor reservoir continence. At least half of the patients who complain of varying degrees of fecal incontinence date the onset of their difficulty to some surgical procedure. Of course, many of these opera-

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tions have been lifesaving measures, and the resulting incontinence is an unfortunate sequel. Many of these patients with fecal incontinence can be rehabilitated and restored as useful members of society by a systematic plan of nonsurgical treatment, consisting of diet, drugs, irrigation of the lower part of the intestine, exercises for the anal muscles, and psychotherapy. These measures are used singly or in combination, as each patient's particular problem dictates.

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SPECIFIC MANAGEMENT FOR LUMBAR AND SACRAL RADICULITIS

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Many cases of low back pain are caused by hyperextension of the lumbosacral part of the vertebral column. They are associated with signs of compression or irritation of the lumbar or sacral nerve roots and with pain radiating down the course of the sciatic nerve. The history frequently reveals an injury, as from lifting, and examination reveals local muscle spasm. The conservative program of treatment for this condition consists of five successive steps: maintenance of proper position while lying in or getting out of bed, next certain exercises of abdominal and gluteal muscles in bed, then certain exercises while standing and walking, later more strenuous exercises in the lying and standing positions, and finally attention to specifc postural problems related to the patient's occupation. He must learn ways to carry out his normal work without extending the lower segments of his vertebral column. The crux of the program is the pelvic tilting associated with this undesired extension. Two case histories illustrate the effectiveness of the program. Of 247 patients with low back pain and sacral or lumbar radiculitis, only 18 failed to respond to this conservative treatment.

In following the literature and in observing practices in other institutions, we have become aware of the need for a specific conservative program for the care of hyperextension derangements of the lumbar spine, associated with lumbar or sacral radiculitis. Furthermore, there is a need for general agreement as to what constitutes a conservative program for these cases. Almost every orthopedist and neurosurgeon today recognizes the value of delaying operation until other means of cure have been exhausted. However, there is little agreement as to what constitutes the other means. Consequently, we see learned articles containing the useless phrase "conservative measures failed." Careful inspection may reveal that the surgeon had no logical plan of treatment or consistent plan from one case to the next. Frequently the conservative plan that failed was gross neglect or physical therapeutic procedures from which one might expect failure or even worsening of the condition.

There is also a great need for careful consideration of the preventive aspects of low back disease. This very common disorder accounts for many hospital visits and represents a tremendous loss to industry in terms of disability. A thorough understanding of the mechanisms of this large group of low back disorders should lead to a general agreement as to measures which may be depended upon to prevent disabling symptoms. We believe that, to a large extent, this knowledge is available to us at the present time and needs only to be agreed upon and put into practice.

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If one takes the article by Goldthwait [1] in 1911 as an arbitrary point of beginning, he finds that at this time the situation in regard to the hyperextension derangements of the lumbar spine was fairly well understood. Even the problem of the protruded disk was discussed, although it was not until much later that it was described as clinical entity by Mixter and Barr.[2] The part of Goldthwait's work that interested us the most is that on his understanding of the ill-effects of extension of the spine in these cases. In his case, this resulted in paraplegia.

In the innumerable articles that have appeared in the last 40 years on the low back problem, it is surprising how these orginal observations have been forgotten. Some authors have shown some understanding of this, but the larger number seem to have passed over this logical approach to the problem in favor of programs and methods which at times are illogical and even harmful. Williams [3] has probably done more than any recent author to clarify our understanding of this type of back syndrome. His program is complete, logical, and effective and should be accepted by all as the only conservative program in the treatment of extension derangement of the low back, associated with lumbar or sacral radiculitis.

Fig. 1.—Mechanisms of encroachment on fifth neural foramen.

Types and Causes of Disorders

In our hospital, as in most general hospitals, there is always a large number of patients confined because of symptoms relating to disorders of the low back. In order to gain any useful concept as to the nature of this problem and its management, we feel it is necessary to separate out certain specific types of disorders that can be fairly accurately diagnosed and thereby avoid the confusion that comes from discussion of all types of low back pain at the same time. The cases that we are going to discuss are cases of low back pain due to hyperextension of the lumbar spine and which are associated with compression or irritation of the lumbar or sacral nerve roots.

Cases of this type are identified by the presence of low back pain associated with pain radiating down the course of the sciatic nerve. The history may reveal an injury, as from lifting, and frequently shows the phenomenon of pain on coughing or from other maneuvers which raise the pressure of the spinal fluid. The examination usually shows a stoop and a list and palpable muscle spasm in the erector spinae muscles. There is tenderness over the involved spinal foramen and pain on stretching the sciatic nerve as in the straight leg raising maneuver. More severe cases show loss of tendon reflexes and sensory defects as well as motor weakness in certain muscles.

The syndrome which has been described may be caused by a variety of pathological conditions. However, each of these conditions has one characteristic in common and that is an ability to cause compression or irritation of the lumbar or sacral nerve roots. This, in addition, is known to be caused by a common mechanism which is an encroachment upon the neural foramen by forces which tend to tilt vertebral bodies posteriorly. This occurs in hyperextension of the spine, and the group of conditions causing these symptoms can be spoken of as hyperextension derangements of the spine (fig. 1).

Our present concept regarding the etiology of this syndrome is that at least five different pathological conditions can produce the same set of symptoms. As will be seen later, we feel that the same therapeutic approach is applicable in this syndrome, even though the etiology may vary from case to case.

The simplest and most comon cause of this condition is known as the facet syndrome. In these cases the facets of the first sacral vertebra are forced upward into a position of subluxation in relation to the lower facets of the fifth lumbar vertebra. This produces encroachment on the foramen in addition to stretching and irritation of the capsule of this small joint. The resulting irritation of the nerve root in the foramen is responsible for most of these symptoms.

Another very common cause for the syndrome, and one which may be a sequel of the facet syndrome, is osteophytosis of the spine, in which osteophytes form around the small apophyseal joints

causing encroachment upon the neural foramen. This, of course, is known as osteoarthritis of the lumbar spine and is frequently attributed to repeated trauma, wear and tear, or general degenerative conditions.

The third less common cause for this syndrome is the forward displacement of one vertebra associated with a defect in the pedicle known as spondylolisthesis. This again causes posterior tilting or hyperextension, encroachment upon the neural foramen, and the syndrome as described previously.

A fourth cause for the syndrome is a protrusion or extrusion of the intervertebral disk substance into the foramen. This, again, may cause irritation or compression of the nerve root and produce the same syndrome. How important this cause is numerically in comparison to the first two is not known. We believe that it accounts for fewer cases than was once thought. We also believe that once it is well established that extrusion of the disk has taken place, the prospect for relief without surgical intervention is poor.

A fifth cause for this syndrome, which we believe properly belongs here, is lumbar laminectomy itself, for, although the offending disk protrusion has been removed, certain structural changes have taken place which make for an even greater tendency to posterior tilting or hyperextension than had existed before. The situation may change from a threat of nerve root compression to one of simple nerve root irritation. However, these patients need the protection that comes from a logical conservative back program.

Method of Treatment

St. Joseph Mercy Hospital, Ann Arbor, Mich., is a general hospital. It is an open staff hospital, where private practitioners of medicine and surgery care for their patients in an independent fashion. Under these circumstances, if a common form of treatment for a specific condition is to be used generally throughout the hospital, it must be one that meets the approval of all the private practitioners who are called upon to treat such a condition. Most of the patients with back conditions of the type under discussion are treated on one of three services—orthopedics, neurosurgery, or physical medicine. The six specialists involved in the three departments named have agreed upon the following method of treating hyperextension derangements of the low spine associated with lumbar or sacral radiculitis.

The patient who presents himself and on whom a diagnosis of hyperextension derangement of the low spine with lumbar or sacral radiculitis has been made, and who is so disabled by the condition as to require hospital care, is put to bed in a section of the hospital where the nursing staff is well acquainted with the kind of care required for this type of patient. We feel that this is extremely important, for, if we are to be logical in our management of this condition, we must recognize that a momentary deviation from our plan of treatment may cause hyperextension of the spine and may produce injury to nerve roots that will prolong the patient's disability for several days or weeks. The nursing staff, therefore, must be instructed thoroughly in the importance of bed positioning and proper methods of getting a patient out of bed. They must know the disastrous effect that may come from placing a patient in the prone position on a bed for a back rub at bedtime.

The bed is prepared with bedboards which are hinged so as to allow the bed to be put into a jackknife position. Intermittent pelvic traction is applied which may contribute to the widening of the neural foramen, but, if nothing else, it definitely assists in maintaining the patient in the therapeutic jackknife position. The jackknife position itself is extremely logical. It makes use of the weight of the patient's trunk in producing flexion of the low spine. If one's diagnosis is correct, this logical positioning should be insisted upon, even in the occasional patient who may object to it, or one must consider a different diagnosis. In the initial phases, adequate sedation and pain relief must be obtained through the use of drugs and heat, and release of muscle spasm must be encouraged by addition of light massage to lumbar muscles. The doctor should avoid repetitious diagnostic tests, such as the prone thrust or straight leg raising, which are dependent on reproducing the irritation of the involved nerve roots. Depending upon the patient's particular condition, he may be allowed to rest in this position without additional attention for 24 to 48 hours.

Following is a program of exercises for treatment of hyperextension derangements of the lumbar spine. This program should be used by therapists as a guide.

STEP 1.—The patient should be instructed to avoid extension of the spine while he is in bed or out of bed. He should be taught how to maintain the proper position in bed and how to get out of bed without extending the lumbar spine. When necessary, the therapist should remind the nurse of the importance of these procedures in the total care of the patient with disease of the low back.

STEP 2.—The patient, lying flat on his back and with the knees bent and soles of the feet flat on the table, should (*a*) learn to tilt the pelvis, exercising the abdominal and gluteal muscles; (*b*) with the pelvis tilted (lumbar spine flat), straighten one leg at a time, returning it to the bent position; (*c*) with pelvis tilted, raise the head and shoulders, then lower them, keeping the back flat; and (*d*) bring the knee towards the axilla, assisting with the hands and arms.

STEP 3.—In the standing position with the heels four to six inches from the wall and the back against the wall, the patient should (*a*) flatten his back against the wall; (*b*)

tilt pelvis (flex lumbar spine) and raise legs alternately; (*c*) stoop, raise trunk, and keep back flat; (*d*) with pelvis tilted, move out from wall, rise up on toes, and return to wall; and (*e*) with pelvis tilted, walk.

STEP 4.—The patient should (*a*) while lying flat on his back and with the knees bent and the soles of the feet flat on the table, touch fingers to toes; (*b*) do straight leg raising, with the back flat; (*c*) with face down, flex one knee under the abdomen in order to maintain flexion of the lumbar spine, with the opposite hip hyperextended, counteracting any flexion deformity in the hip, and then alternate sides; and (*d*) from the standing position the patient is taught to squat with the feet flat on the floor.

STEP 5.—In this part of the exercise program, the therapist will consider specific postural problems encountered in the patient's work. Recommendations will be made according to needs.

The physical therapist is called upon to initiate a program of back exercises beginning with step 1, which is simply instruction in positioning and ways to get out of bed without extending the lumbar spine. On order from the attending doctor, the

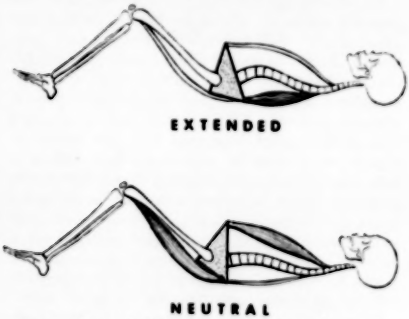

Fig. 2.—Effect of abdominal and gluteal muscles in maintaining proper alignment of lumbar region of spine.

therapist then moves to steps 2, 3, and 4 of the progressive program of back exercises, which follows quite closely to the recommendations of Williams. These exercises are designed first to relieve, by stretching, some of the muscle and ligamentous tightness contributing to the hyperextension of the spine. Second, they are designed to strengthen the flexors of the low spine and, finally, to teach postural habits which will be helpful in allowing the person to resume normal activities and prevent future attacks of back pain. As a fifth step, the physical therapist considers some special problems of the patient's occupation that may be important. These may be corrected or accommodated.

In the first step of the exercise program, which is done in conjunction with the physical treatment already instituted, the therapist begins active and passive stretching of the posterior muscles and ligaments. This is accomplished by having the patient pull his knees, one at a time, towards the axilla. Not only can a patient with acute symptoms do this with relative ease but he frequently obtains considerable relief of pain by this maneuver. The therapist may assist, thereby adding further force towards widening the neural foramen. At this point, the patient is taught to tilt the pelvis so as to produce flexion of the lumbar spine. The physical therapist does this by demonstrating the function of abdominal and gluteal muscles in this exercise (fig. 2).

The crux of the whole program is this pelvic tilting or spinal flexion, and all subsequent exercises are done from this position. All subsequent activity is done with the spine held in this position. In this second step, the therapist also begins to teach the patient strengthening exercises for the flexors, beginning by a simple head raising, followed by trunk raising, and keeping the lower spine flattened throughout the entire maneuvers.

Depending on the patient's progress, the therapist is then ordered to begin the third step in the exercise program which has to do with standing. We feel very strongly that if a patient is asked to get out of bed and stand, when he has already shown evidence of compression or irritation of a nerve root, that he should be taught first how to get out of bed properly, and secondly, how to stand properly, so as not to reproduce this injurious condition. Many times we have seen a patient, after a period of bed rest in a jackknife position, become essentially symptom free and then be asked without instruction to get up and see if he could go to the bathroom. This, of course, frequently led to recurrence of the symptoms and to a loss of several days or weeks of the patient's time. The therapist therefore teaches the patient to get out of bed without extending the spine and teaches him to walk with the spine in a neutral or flexed position. This is done by proper instruction in the use of the gluteal and the abdominal muscles in maintaining this favorable position of the low spine.

If this is well tolerated, the patient is taught to stoop and resume the standing position without extending the spine. Extending the lumbar spine first is frequently a natural way of assuming the standing position, especially in a person with weak abdominal muscles. If the patient is still showing improvement, one can be quite sure at this point that he will respond satisfactorily to this conservative program, and he is begun on the fourth step in the progressive exercise routine which allows for further heavy resistance exercises for his flexors and gluteals and vigorous stretching of any residual hip flexion contractures which may be a limiting factor in producing adequate flexion of the lumbar spine when walking in the upright position.

Assuming that this patient has responded satisfactorily throughout this program, he is now about to leave the hospital. The therapist turns her attention to specific hazards that may be present in his occupation. She teaches him ways to carry out his normal work without extending the low back. Certain tricks may be very useful, such as keeping the knees higher than the hip joints, for stenographers or people who are required to drive an automobile in their work. In all of these cases, we feel that the important thing is to make the patient aware of what it means to extend the low spine and provide him with the adequate muscle strength to counteract this tendency. This, we feel, takes more time and attention than most physicians and surgeons can give their patients, and we expect the physical therapist to so train the patient by repeated sessions that he understands this very thoroughly.

After the patient has been discharged from the hospital, the physical therapist will be asked to see him at lengthening intervals in order to see that he maintains the strength and postural habits that he has been taught. Some of these patients may be sent home with a brace or other type of low back support, but, in general, we feel that the chief use of such an appliance is to remind the patient to maintain the proper postural alignments that he has been taught.

A certain number of patients, particularly those with an extruded intervertebral disk and some of those suffering from far advanced spondylolisthesis will not respond to this program and probably will not be carried much beyond the second step in the treatment. If this is found to be the case and we are sure that no mistakes have been made by the nurse or therapist in following this logical program, it can be used as an important diagnostic point in deciding on subsequent treatment. However, unless this program has been followed logically in every detail, we see no value in using it as a diagnostic criterion.

Of 247 patients with low back pain and with sacral or lumbar radiculitis admitted to this hospital in 1956, 18 failed to respond to the conservative program and were subsequently operated on for removal of an extruded intervertebral disk. This is a rate of 7%, which we believe speaks favorably for the conservative program that we use in our hospital.

Of 33 consecutive admissions for this type of back condition during a two-month period, 25 were admitted to the orthopedic service, 5 to physical medicine, and 3 to neurosurgery; 22 were men and 11 were women. Their ages ranged from 21 to 65. The causative factor was lifting in 13 and a fall or a blow in 7, and in the others the condition was described as coming on gradually. Seven of the 33 were given a final diagnosis of herniated intervertebral disk, and these showed objective signs of nerve root compression. One of the seven who had been given a diagnosis of herniated disk underwent a laminectomy for removal of the extruded disk. Some part of the progressive back program was used in all of these patients. The progressive exercises were used in 29 of the 33 patients. Exercises were begun the first day in 11 cases and on the second to the fourth day in 10 cases. The time of beginning the exercises in the remaining varied from the 5th to the 19th day.

These data show the acceptance of the program by the several services treating this type of patient. Two types of patients frequently are neglected as far as the exercise program is concerned. The one is the patient who enjoys a rapid recovery on simple bedrest alone, and the other is the one showing definite and severe signs of nerve root compression and in whom any motion is painful. The incidence of laminectomies noted above is essentially the same for the whole year.

Report of Cases

Case 1.—A 20-year-old man was admitted to the hospital because of pain in the low back, in the right hip, and behind the right knee. The onset of these symptoms occurred five months before, after the patient had worked at driving a tractor for several weeks. The symptoms had been intermittent, and he had experienced one short period of relief of pain about six weeks before coming to the hospital. The pain was made worse on coughing, and certain movements reproduced the acute pain. The patient stood with a list to the left. The straight leg raising sign was positive at 40 degrees on the right and 55 degrees on the left. Tendon reflexes show diminution of patellar and Achilles reflexes on the right as compared to the left. There was no sensory defect noted.

This patient was put to bed in the jackknife position, and pelvic traction with 15 lb. of weight was started. He had physical therapy consisting of moist packs and massage to his low back on the day of admission, and this was continued twice daily during his hospital stay. The physical therapist was instructed to begin progressive back exercises on the third hospital day. The patient was having continuous pain, and the back exercises were discontinued on the fifth hospital day, since it was suspected the exercises were contributing to his pain. On the seventh hospital day the exercise program was reinstituted, and the patient steadily improved. He was discharged from the hospital at the end of two weeks. At this time the examination showed the tendon reflexes to be equal bilaterally in the legs. The straight leg raising sign had improved to allow 90 degrees of flexion on the left and 60 degrees flexion on the right. The patient was discharged with a chairback brace and instructed to continue his back exercises three times daily.

The patient was seen in the physical therapy department after two weeks for follow-up instructions in his exercise program. He had remained improved, experiencing only minimal soreness in his low back. Two months after discharge from the hospital the patient was symptom free. There were no neurological signs in his legs. He was advised to discontinue the use of the brace and to continue a modified exercise program for an indefinite period of time.

CASE 2.—A 48-year-old man experienced onset of acute pain in his back after a game of touch football with his sons, one week before admission. This pain was made worse on coughing. The patient recalled an episode nine years previously, following a lifting injury, which was similar to the current episode of pain. Examination showed the patient to have a fixed low spine with a slight list to the left. Straight leg raising from the supine position produced severe pain at 20 degrees on the right and at 60 degrees on the left. There was no sensory loss or change in reflexes noted.

The patient was put to bed in the jackknife position, and pelvic traction with a 15 lb. weight was applied. On the day after admission, therapy was started with hot packs and massage to the low back, and the patient was given instruction in the first two steps of the progressive back program. The patient was considerably improved on the third hospital day. He was fitted with a canvas back support and on the fourth day he was sent home to continue his rest and exercises there.

The patient had his bed at home prepared in a jackknife position and was quite familiar with the exercise program. He was allowed to be up part of the day. In two weeks he was seen again, at which time he had slight discomfort in his back. He was standing straight. The straight leg signs showed pain at 50 degrees on the right; the left was normal. There were no reflex changes or sensory losses. The patient was advised to continue his exercises and to begin to discontinue the use of the corset.

Two months later the patient called and described a recurrence of his pain. He stated that he had discontinued doing his exercises two weeks previously because he was entirely free of symptoms. He was advised to spend two days in bed in the jackknife position and to resume the back exercises. The symptoms were relieved after two days, and the patient has been advised to continue a modified back exercise program indefinitely.

Comment

The need is great for agreement as to what constitutes a proper conservative program for hyperextension derangements of the lumbar spine. In a recent article by Monro,[4] a conservative program is described as one including such things as manipulation and hyperextension, which is quite contrary to our feelings in this matter. Key,[5] in a discussion of disk lesions of the lumbar spine, described a conservative program as being one of time and rest. There is considerable wisdom in this idea, since most of the things that are done in a conservative program are directed towards local rest of the nerve root. However, one should be specific in setting forth the criteria of an adequate conservative program. Williams describes a conservative treatment as doing the following: (1) reducing the lumbosacral angle and thereby lifting the weight from the posterior structures at this site, (2) actively developing those muscles whose action is that of lumbosacral flexion, (3) passively stretching those muscles whose action is extension of the lumbosacral spine, and (4) maintaining correct postural attitudes in standing, walking, working, sitting, and sleeping.

He sums this up with a phrase "Learn to live 24 hours a day without a hollow in the lower part of your back." It would seem to me that we could do no less than agree on this as the proper conservative program, and unless this method had been used, one would not be able to say that "conservative measures failed."

Knowing what we do about the effect of postural control on the very common disabling condition that we have discussed, it seems that the preventive aspects should be stressed in schools and industry. Many school children are required to hyperextend the spine far beyond the limits of the structures there, thereby setting the stage for future disabling back conditions. The medical profession across the nation should take an interest in this part of the school program the same as they take an interest in such procedures as immunization and correction of defective sight and hearing.

The medical profession should also agree on these things and work with industry so as to eliminate the many hazardous positions that workers are required to assume. We note, for instance, a worker who operates a foot lever from a high stool or a stenographer who has been taught to hyperextend the spine. These positions, when they are assumed by people driving vehicles or airplanes, have the added hazard that comes from sudden bumps and shifting of positions.

Summary

A logical and effective program for a common type of low back condition, which may be called hyperextension derangement of the lumbar spine, has been used in a typical general community hospital. We believe that this program should be studied and agreed on by all physicians called on to treat these cases. Fewer patients will then be required to undergo surgery, and the medical profession will be able to exert a beneficial influence for the public health by working with the schools and industry in prevention of this type of disease.

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PLASMA TRANSFUSION WITHOUT TRANSMISSION OF SERUM HEPATITIS

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Because of concern over ability to cope with the virus of hepatitis, much blood plasma is currently being wasted. The storage of liquid plasma at room temperature for six or more months eliminates activity of the virus of hepatitis. The method is simple and adaptable to existing blood bank facilities, and it permits the pooling of plasma to avoid blood group (ABO) considerations.

Plasma is the best substitute available for whole blood transfusion in a variety of clinical conditions, such as hypovolemic shock and the chronic depletion in blood volume which occurs in protracted gastrointestinal diseases and severe burns. Other important uses of plasma lie in parenteral protein feeding and in the correction of some defects in the clotting mechanism.

During World War II, it was learned that the virus of serum hepatitis from human carriers was being disseminated in pools of plasma and was producing serum hepatitis in a high percentage of the recipients.[1] This discovery discouraged the use of plasma and has been followed by a serious delay in the preparation of a safe plasma for civilian and military needs. Divergent efforts to circumvent this problem have consisted of attempts to destroy viral activity with chemicals, ultraviolet irradiation, or prolonged storage of liquid plasma at room temperatures; of a return to use of group-specific plasma; and of substitution of virus-free protein fractions of plasma and unnatural plasma-volume expanders.

The use of ultraviolet irradiation was a costly failure, as evidenced by experience during the Korean war and subsequent laboratory and clinical investigations.[2] The addition of chemicals has yet to reach the stage of application. The use of group-specific plasma is a cumbersome expediency which introduces direct matching as a safety requirement and imposes production problems related principally to testing for sterility and to clarification procedures. Methods for preparation of fractions waste albumin and other proteins are impracticable for blood banks supplying community needs and inflict serious problems of cost for more centralized programs. Moreover, fractions must be supplemented with other components of whole plasma in the treatment of patients. The defects and hazards of the unnatural plasma expanders permit only limited use.

Present limitations on the storage of red blood cells and an increasing demand for concentrated cell preparations in the treatment of anemias have created a vast natural resource for blood plasma in an ever-growing number of hospital and community blood banks, and much of this plasma is currently being wasted. Achievement of a good plasma product has lagged because of concern over ability to cope with the virus of hepatitis. Concurrently, a large amount of plasma which should be salvaged is being thrown away, due to lack of demand from physicians because of fear of hepatitis.

The ideal blood substitute is one which most nearly approaches whole plasma in content, is free of bacterial and viral contamination and pyrogens, is low in antigenicity and incompatible antibody titer, and can be prepared without prohibitive costs in equipment and procedure. The method of preparation should be adaptable for use in large and small operations in order to accommodate daily patient needs through the existing blood bank facilities, as well as needs in local and national disasters.

The University of Cincinnati Blood Transfusion Service has been supplying the plasma needs of a large community since 1941.[3] After we had run the gamut from the use of large pools to small pools of six units, to the purchase of irradiation equipment, and finally to use of group-specific plasma in attempts to minimize the occurrence of hepatitis, our attention was drawn in 1951 to Allen's proposal that the storage of liquid plasma at room temperatures for six or more months inactivates the virus of hepatitis insofar as human transmission of the disease is concerned.[4]

Thus, there were strong incentives for investigation of this method by subjecting it to prolonged clinical trial. An opportunity to regain the advantages of pooling and yet inactivate the virus of hepatitis was attractive, providing the other points of suitability of plasma could be maintained in the process. A program planned to determine the value of Allen's method was begun in January, 1952. A preliminary report having been made elsewhere,[3b] the purpose of this paper is to give the results of the completed investigation for the four-year period of January, 1953, to January, 1957.

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Method

Plasma was prepared from pooled blood of 30 to 72 donors and stored at room temperatures (72 to 95 F) for six months before release. All plasma was obtained from carefully screened donors, and the processing conformed to the standards of the National Institutes of Health, except that the requirement of ultraviolet irradiation was not employed. Details of the method of preparation and of the pyrogen, bacterial, and hemoglobin controls are recorded elsewhere.[3b] Bacterial contamination was detected in less than 1% of the plasma, human pyrogen tests were negative for all lots, and transmission of bacterial disease was not encountered.

Storage was begun in January, 1952, the first lot was issued in July, and contact with recipients began in January, 1953. It has taken a long time to accumulate enough data to be of value; plasma was requested infrequently because of the fear of hepatitis, and the group of patients subjected to this risk had injuries and diseases which often resulted in early death.

The survey for incidence of jaundice began with a form letter and questionnaire sent to each recipient six months after transfusion. Later, a house visit was made by a graduate nurse to confirm the information supplied. Detailed records were kept, and the data were tabulated.

Transfusion Data in Six Cases of Hepatitis

Case	Units of Plasma*	Donors of Plasma, No.	Units of Whole Blood
1	1	32	1
2	3	66	9
3	2	49	1
4	1	43	1
5	1	76	4
6	3	132	2

* No two patients with hepatitis received plasma from same lot.

Data and Results

In the entire study there were 1,638 recipients of plasma from pools with a donor population of 5,486. There were 556 early deaths, leaving 1,082 persons believed still living and available for follow-up study. Data were obtained for 845 of these. The donor population of the whole blood received by the group of 845 totaled 1,991, while the donor population of the plasma totaled 5,447. The donor exposure remained high in the 845 followed patients because the survivors received transfusions from all but one of the pools of plasma. Six persons of the 845 developed jaundice. Recipients were then divided into two groups: group 1 received plasma and whole blood; group 2 received plasma only.

Results in Group 1.—In group 1 there were 1,150 recipients of plasma from pools with a donor population of 5,352. These patients also received 4,059 units of whole blood. There were 401 deaths, leaving 749 for follow-up. Contact was made with 563. These 563 patients were exposed to a plasma donor population of 5,352 and to 1,991 units of whole blood. The six who contracted jaundice were in this group.

The cause of hepatitis in these six can only be surmised, since each received whole blood and plasma (see table). They received 1, 9, 1, 1, 4, and 2 units of blood, respectively, and 1, 3, 2, 1, 1, and 3 units of plasma. No two of the patients with jaundice received plasma from the same lot. Of 72 patients followed who received plasma from these same lots, none contracted hepatitis.

The hepatitis occurred in a group of 845 followed patients who received 1,991 units of whole blood, an incidence of infectivity of 0.30%, which could be expected from the whole-blood exposure. The group of 845 was also exposed to plasma of 5,447 donors. If the plasma were responsible, the incidence of infectivity would be 0.11%. This figure is contrary to all experiences with untreated or irradiated pools of plasma, being even lower than that encountered with group-specific plasma or whole blood.

Analysis of results to this point indicates that the blood was most likely responsible for the jaundice and that strong evidence exists that the stored plasma can be used with reasonable safety.

Results in Group 2.—The most positive information concerning the safety of this plasma comes from analysis of results in recipients of plasma only. In this group there were 488 recipients of plasma from pools with a donor population of 5,157. There were 155 deaths, leaving 333 for follow-up. Data were definite in 282. Among these, no jaundice occurred, although the patients were exposed to plasma of 4,892 donors. Here, 89% of the entire plasma-donor population is converted to donor-exposure of 282 recipients who were followed. None received whole blood and none developed hepatitis.

These results were substantiated by a review of charts of patients with hepatitis in Cincinnati hospitals. This review failed to produce a single recipient of plasma who had developed jaundice and who had escaped the follow-up.

Comment

This study shows that the method of Allen is a practicable and effective solution to the plasma-hepatitis problem. The inability to detect hepatitis in 282 recipients exposed to the plasma of 4,892 donors is in sharp contrast to all previous experiences with untreated and irradiated pooled plasma, in which the infectivity has ranged from 1% in small pools of six or eight up to 22% in larger pools.[3] In addition to the effect on the virus of hepatitis, the method has permitted a return to pooling and has removed the limitations imposed by the use of group-specific plasma, a program

which had been adopted by force of necessity between 1949 and 1952. The introduction of direct matching as a safety requirement had eliminated one of the most important advantages of plasma, use in the treatment of shock while waiting for whole blood to be matched.

During the time of this study, adequate clinical experience has been gained in the department of surgery of the University of Cincinnati to attest to the suitability and effectiveness of this plasma. In the laboratory no new problems in sterility and pyrogen controls are introduced. Plasma which is kept sterile and free of pyrogens during the processing will remain so for an indefinite period in the standard final containers. Less than 1% of the plasma prepared during the time of this study was discarded due to bacterial contamination. Human pyrogen tests were negative for all lots, and transmission of bacterial disease was not encountered. The alteration in albumin induced by storage of plasma as a liquid for months is minor.* There is no apparent effect on the clinical response.

Much of the value of Allen's method lies in its simplicity, making it possible for many blood banks to salvage plasma from outdated blood which is now being wasted. In the event of need for large stockpiles for use in mass casualties, plasma stored as a liquid for six or more months can be frozen and dried and kept indefinitely.

Summary

In a clinical trial which exposed 282 patients to the plasma of 4,892 donors, the storage of liquid plasma at room temperatures for six or more months eliminated activity of the virus of hepatitis. This plasma is now being given to patients without concern for the transmission of serum hepatitis. The method is simple and adaptable to existing blood bank facilities, and it permits the pooling of plasma to avoid blood group (ABO) considerations. In its use, ordinary safeguards should be employed to insure the other requirements for suitability of plasma.

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FRACTURES OF NECK OF FEMUR.—In routine hip fractures a successful hip-nailing is more desirable and gives a better end-result than a replacement prosthesis. However, we feel that in certain selected cases of neck fractures, the nailing of the hip by the conventional method carries a calculated risk with it insofar as undesirable results are concerned. . . . The advantages of [the insertion of an endoprosthesis] as a primary procedure include early ambulation, reduction of hospital stay, reduction in the cost of the injury, reduction of complications, and easier nursing care. All patients were operated upon by the posterior approach, with no major complications. Most of our patients have been able to take care of themselves in their homes, using a cane as an aid.—A. A. Savastano, M.D., L. A. Sage, M.D., and Vincent Zecchino, M.D., Treatment of Fresh Fractures of Neck of Femur with Intramedullary Stem Prostheses, *A. M. A. Archives of Surgery*, December, 1957.

SMOKING AND DEATH RATES—REPORT ON FORTY-FOUR MONTHS OF FOLLOW-UP OF 187,783 MEN

II. DEATH RATES BY CAUSE

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The death rates from specific causes have been studied in relation to smoking habits in a group of 187,783 men between the ages of 50 and 69. During the period of the study 11,870 of these men died. For microscopically proved cases of cancer as well as for the total cases reported as cancer it was found that the death rates were higher among regular cigarette smokers than among men who never smoked, that the mortality ratio increased with the number of cigarettes smoked per day, and that the death rates were higher among pipe and cigar smokers than among men who never smoked. A total of 7,316 deaths occurred among regular cigarette smokers, an excess of 2,665 over the 4,651 that would have occurred had the age-specific death rates for smokers been equal to that for nonsmokers. Coronary disease accounted for 52.1% of the excess; lung cancer accounted for 13.5%, and cancer of other sites likewise for 13.5%. An extremely high association between cigarette smoking and death rates for men with lung cancer was found in rural areas as well as in large cities. The most important finding of this study was the high degree of association between cigarette smoking and the total death rate.

Between Jan. 1 and May 31, 1952, information was obtained on the smoking habits of 187,783 white men between the ages of 50 and 69 who were then traced through Oct. 31, 1955. During this period of time, 11,870 of the men died. The total experience covered 667,753 man-years. As described in part 1 of this paper,[1] we found that the total death rate (from all causes combined) was much higher among men with a history of regular cigarette smoking than among men who had never smoked cigarettes regularly and that the death rate increased with amount of cigarette smoking. Part 2 of this study is concerned with death rates from specific causes in relation to smoking. Causes of death were ascertained from death certificates, but in every instance that cancer was mentioned we wrote to the doctor, hospital, or tumor registry to obtain more detailed information.

Cause of death as stated on death certificates is subject to error, particularly when the doctor who signs the certificate has little or no opportunity to study the patient before death and no autopsy is performed. We were pleased to find that the diagnosis was confirmed microscopically in 79% of the deaths ascribed to cancer and that in the majority of the remaining 21% the evidence was such as to leave little doubt that death was due to this disease. However, even in microscopically verified cases there is sometimes doubt as to the exact primary site, especially when the disease has already spread widely by the time of first diagnosis. A somewhat analogous situation seems to exist in deaths ascribed to diseases of the heart and circulatory system; that is, many patients suffer from two or more ailments in this class of diseases, and it is sometimes difficult to say which specific condition was the underlying or principal cause of death. Indeed, the wisdom of attempting to make such a distinction has been questioned.[2]

For these reasons, we first made an analysis classifying the deaths into five broad categories: (1) cancer (International Statistical Classification of Diseases, Injuries and Causes of Death list numbers 140-205), (2) heart and circulatory diseases, including vascular lesions of the central nervous system (international list numbers 330-334 and 400-468), (3) pulmonary diseases, including pulmonary tuberculosis, asthma, influenza, pneumonia, bronchitis, and other pulmonary diseases but excluding neoplasms (international list numbers 001-002, 241, 480-502, and 520-527), (4) all other diseases, and (5) accidents, violence, and suicide (international list numbers E800-E999).

From the Statistical Research Section of the American Cancer Society.

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This is the second part of a two-part article appearing in consecutive issues of THE JOURNAL.

General Findings

Table 1 shows the number of deaths and death rates per 100,000 man-years for (1) men who never smoked; (2) men with a history of regular cigarette smoking, many of whom also smoked cigars and pipes; and (3) all other subjects, including pipe

smokers, cigar smokers, and occasional smokers who had never smoked cigarettes regularly. Table 2 shows the number of deaths and death rates for men with a history of regular cigarette smoking only who in 1952 were smoking cigarettes regularly in the following amounts: (1) less than one-half pack of cigarettes a day, (2) one-half to one pack of cigarettes a day, and (3) one pack or more of cigarettes a day. On each of these tables is shown the number of deaths which would have occurred among the men in a particular smoking group if their age-specific death rates had been the same as for men who never smoked. This is designated as the "expected" number of deaths, while the number which actually occurred is designated as the "observed" number. Also shown is the ratio of observed to expected number of deaths (i. e., the mortality ratio). All of the computations were based on rates carried one significant figure beyond what is shown on these tables. The expected number of deaths was then rounded off to the nearest whole number. Significance tests were based upon the chi-square test, with expected values computed from the combined age-specific death rates for the nonsmokers and the smoking group in question. Table 3 shows the observed and expected number of deaths for (1) men with a history of occasional smoking only, (2) men with a history of pipe smoking only, and (3) men with a history of cigar smoking only.

The death rates from accidents, violence, and suicide were about the same for men with a history of regular cigarette smoking as for men who never smoked (fig. 1). The observed number of deaths from these causes among cigarette smokers was 363, compared with 385 expected deaths, a difference of 22. This difference is not statistically significant

TABLE 1.—*Number of Deaths and Death Rates Per 100,000 Man-Years by Cause of Death and by Age at Start of Study for Men Divided into Three Groups by Smoking History**

Cause of Death	Smoking History	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected† No. of Deaths Observed	Expected	Ratio
Total: all causes	None	218	656	375	1,139	438	1,575	613	2,800	1,644	...	1.00
	Cigarette	1,633	1,117	2,040	1,699	2,016	2,958	1,627	4,013	7,316	4,651	1.57
	Other	280	691	592	1,277	878	1,861	1,230	3,170	2,980	2,563	1.14
Cancer	None	35	105	65	197	67	241	91	416	258	...	1.00
	Cigarette	270	180	430	358	478	707	326	804	1,490	741	1.97
	Other	42	104	112	242	161	362	216	566	531	460	1.33
Heart and circulatory diseases	None	129	388	217	659	285	1,025	427	1,951	1,058	...	1.00
	Cigarette	1,024	701	1,347	1,099	1,255	1,891	1,067	2,622	4,593	2,924	1.57
	Other	167	412	368	794	537	1,207	800	2,096	1,872	1,663	1.13
Coronary artery disease	None	90	271	142	431	204	733	273	1,247	709	...	1.00
	Cigarette	765	524	962	803	921	1,219	713	1,750	3,361	1,973	1.70
	Other	113	279	253	546	348	782	513	1,344	1,227	1,112	1.10
Other heart diseases	None	39	60	37	112	39	140	52	238	148	...	1.00
	Cigarette	112	77	131	109	131	173	129	318	503	425	1.18
	Other	26	64	53	114	78	175	105	270	300	230	1.13
Cerebral vascular lesions	None	16	48	31	94	32	115	85	398	164	...	1.00
	Cigarette	104	71	123	102	152	201	177	437	556	428	1.30
	Other	21	52	52	112	96	216	161	422	330	263	1.25
Other circulatory diseases	None	3	9	7	21	10	36	17	78	37	...	1.00
	Cigarette	43	29	31	26	51	68	48	118	173	97	1.78
	Other	7	17	10	22	15	34	23	60	55	59	0.93
Pulmonary diseases (except neoplasms)	None	2	6	8	24	7	25	13	59	30	...	1.00
	Cigarette	38	26	68	57	71	94	54	133	231	81	2.85
	Other	5	12	12	26	23	37	37	97	77	48	1.60
Other diseases	None	28	84	46	140	49	176	52	238	175	...	1.00
	Cigarette	174	119	183	152	188	249	124	306	669	520	1.29
	Other	37	91	62	134	65	146	112	293	276	268	1.03
Gastric ulcer	None	0	0	0	0	0	0	0	0	0	...	1.00
	Cigarette	6	4	16	13	13	17	11	27	46	0	Inf.
	Other	0	0	1	2	2	5	2	5	5	0	Inf.
Duodenal ulcer	None	1	3	4	12	0	0	3	14	8	...	1.00
	Cigarette	14	10	11	9	16	21	13	32	54	25	2.16
	Other	1	3	3	7	5	11	2	5	11	12	0.92
Cirrhosis of liver	None	3	9	2	6	4	14	6	27	15	...	1.00
	Cigarette	30	21	21	18	23	30	9	22	83	43	1.93
	Other	5	12	7	15	8	18	9	24	29	23	1.26
Miscellaneous	None	24	72	40	122	45	162	45	196	132	...	1.00
	Cigarette	124	85	135	112	136	180	91	224	486	453	1.07
	Other	31	77	51	110	59	112	99	259	231	233	0.99
Accidents, violence, and suicide	None	24	72	39	119	30	108	30	137	123	...	1.00
	Cigarette	123	83	112	93	74	98	56	138	363	385	0.94
	Other	29	72	38	82	42	94	45	118	154	185	0.83

* "None" refers to no history of smoking; "cigarette" refers to regular smoking of cigarettes (including additional cigar or pipe smoking); and "other" refers to occasional smoking, cigar smoking, and pipe smoking but no regular cigarette smoking.

† Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of men in each of the other groups

(p=0.22). We divided this category into two groups of deaths: (1) suicide and (2) accidents and violence. Neither of these two groups showed a statistically significant association with smoking habits.

In contrast, 1,460 men with a history of regular cigarette smoking died of cancer, compared with an expected 741 deaths (had the age-specific death rates due to cancer of these men been the same as those of men who never smoked). The mortality ratio was 1.97 (fig. 1). The mortality ratio for cancer increased with the amount of cigarette smoking from 1.87 for men smoking under one-half pack a day to 1.92 for men smoking one-half to one pack a day and to 2.94 for men smoking one pack or more a day (table 2). Both pipe smokers and cigar smokers had higher death rates from cancer than men who never smoked, the mortality ratios being 1.44 and 1.34 respectively (table 3).

The deaths of 4,593 cigarette smokers were attributed to diseases of the heart and circulatory system, as compared with 2,924 expected deaths, a difference of 1,669. The mortality ratio was 1.57 (fig. 1). The mortality ratio for these causes increased with amount of cigarette smoking from 1.27 for under one-half pack a day to 1.74 for one-half to one pack a day and to 1.95 for one pack or more a day (table 2). For cigar smokers, there were 620 observed deaths from heart and circulatory diseases, compared with 492 expected deaths (mortality ratio, 1.26). This difference is statistically significant ($p < 0.001$). For pipe smokers, there were 485 observed deaths and 454 expected deaths. This difference is not statistically significant (p=0.25).

Only 338 of the 11,870 deaths were attributed to pulmonary diseases other than lung cancer. These showed a high degree of association with cigarette

TABLE 2.—*Number of Deaths and Death Rates Per 100,000 Man-Years by Cause of Death and by Age at Start of Study for Men with History of Regular Cigarette Smoking Only*

Cause of Death	Packs Per Day	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Total: all causes	<½	88	937	110	1,205	131	2,298	141	3,849	470	350	1.34
	½-1	443	1,128	551	1,875	482	2,875	357	4,441	1,833	1,081	1.70
	1+	421	1,408	428	2,280	300	3,280	177	4,714	1,326	658	2.02
Cancer	<½	20	213	33	362	27	474	23	628	103	55	1.87
	½-1	74	189	113	385	79	471	66	921	332	173	1.92
	1+	71	238	105	502	85	929	51	1,358	312	106	2.94
Heart and circulatory diseases	<½	47	501	58	633	84	1,473	93	2,529	282	222	1.27
	½-1	278	708	342	1,164	318	1,897	236	2,936	1,174	675	1.74
	1+	264	883	222	1,348	174	1,993	102	2,736	792	406	1.95
Coronary artery disease	<½	35	373	50	548	49	860	58	1,583	192	149	1.29
	½-1	213	543	258	879	235	1,402	158	1,966	864	456	1.89
	1+	205	679	199	1,065	129	1,411	73	1,944	604	275	2.20
Other heart diseases	<½	6	64	4	47	15	263	12	228	37	32	1.16
	½-1	28	71	42	143	31	185	28	348	129	99	1.30
	1+	29	97	22	118	19	208	11	293	81	61	1.33
Cerebral vascular lesions	<½	3	32	4	47	15	263	19	519	41	33	1.24
	½-1	22	59	30	123	40	239	41	510	140	97	1.44
	1+	27	90	24	128	19	208	13	346	83	57	1.46
Other circulatory diseases	<½	3	32	0	0	5	88	4	109	12	7	1.71
	½-1	14	36	6	20	12	72	9	112	41	22	1.86
	1+	5	17	7	37	7	77	5	133	24	13	1.85
Pulmonary diseases (except neoplasms)	<½	2	21	1	12	5	88	2	55	10	6	1.67
	½-1	9	23	15	51	16	167	15	387	57	19	3.00
	1+	12	40	11	59	10	109	7	186	40	11	3.64
Other diseases	<½	11	117	12	142	13	228	15	410	51	38	1.34
	½-1	54	138	46	157	48	286	27	326	175	123	1.42
	1+	47	157	35	187	21	230	11	293	114	76	1.50
Gastric ulcer	<½	0	0	1	12	0	0	2	55	3	0	Inf.
	½-1	1	3	8	27	6	36	2	25	17	0	Inf.
	1+	4	13	4	21	1	11	2	53	11	0	Inf.
Duodenal ulcer	<½	0	0	0	0	1	18	2	55	3	2	1.50
	½-1	5	13	2	7	6	36	2	25	15	6	2.50
	1+	3	10	3	16	2	22	2	53	10	4	2.50
Cirrhosis of liver	<½	1	11	2	24	3	53	1	27	7	3	2.33
	½-1	9	23	6	20	1	6	3	37	19	10	1.90
	1+	9	30	6	32	2	22	1	27	18	6	3.00
Miscellaneous	<½	10	107	9	107	9	158	10	273	38	33	1.15
	½-1	39	99	30	102	35	209	20	249	124	107	1.16
	1+	31	104	22	118	16	175	6	160	75	67	1.12
Accidents; violence, and suicide	<½	8	85	6	71	2	35	8	218	24	28	0.86
	½-1	28	71	35	119	19	113	13	162	95	92	1.03
	1+	27	90	25	134	10	109	6	160	68	59	1.15

*Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of men in each of the other groups.

smoking. A total of 231 deaths of cigarette smokers were attributed to pulmonary diseases, as compared with only 81 expected deaths (mortality ratio, 2.85). For men smoking one or more packs of cigarettes a day, the mortality ratio was 3.64. The death rate from pulmonary diseases was higher for both pipe and cigar smokers than for men who never smoked; but there were not many cases, and these differences were not statistically significant.

Deaths attributed to all other causes combined (including uncertain or unknown cause of death) accounted for less than 10% of the 11,870 deaths. This group, taken as a whole, showed some association with cigarette smoking, as indicated by the mortality ratio 1.29 (see fig. 1). As will be shown later, a few diseases in this category account for most of this relationship.

TABLE 3.—*Observed Versus Expected* Number of Deaths by Cause for Men with History of Occasional Smoking Only, Pipe Smoking Only, and Cigar Smoking Only*

Cause of Death	Occasional Only			Pipe Only			Cigar Only		
	Observed	Expected	Ratio	Observed	Expected	Ratio	Observed	Expected	Ratio
Total: all causes	686	395	1.69	774	691	1.12	925	761	1.22
Cancer	115	93	1.24	155	108	1.44	169	119	1.34
Heart and circulatory diseases	401	263	1.85	485	454	1.07	620	492	1.26
Coronary artery disease	259	257	1.01	312	306	1.02	420	329	1.28
Other heart diseases	60	54	1.11	70	62	1.13	80	68	1.18
Cerebral vascular lesions	72	59	1.22	93	73	1.27	101	77	1.31
Other circulatory diseases	10	13	0.77	10	17	0.59	19	17	1.12
Pulmonary diseases (excluding neoplasms)	29	11	2.64	23	13	1.77	18	14	1.29
Other diseases	67	63	1.06	71	71	1.00	86	80	1.08
Gastric ulcer	0	0	....	2	0	Inf.	2	0	Inf.
Duodenal ulcer	3	3	1.00	5	3	1.67	1	4	0.25
Cirrhosis of liver	7	6	1.17	5	6	0.83	12	7	1.71
Miscellaneous	57	55	1.04	59	62	0.95	71	70	1.01
Accidents, violence, and suicide	31	44	0.77	40	48	0.83	41	56	0.73

* Calculated by applying the age-specific death rates of men who never smoked to the man years of exposure to risk of men in each of the other groups.

Cancer

Malignant neoplasms were mentioned on 2,326 death certificates, and in each instance we wrote to the doctor, hospital, or tumor registry for further information. We sought similar information on 24 cases in which death was attributed to a benign neoplasm. Replies were received for 2,242 (95%) of the cases. Five cases recorded as benign neoplasm on the death certificate were found to be malignant tumors of the brain, and six cases recorded as cancer were found not to be cancer on the basis of further evidence. Making use of this data, we classified 2,249 (18.9%) of the 11,870 deaths in the study as due to cancer and an additional 75 as due to some other cause with cancer present. Of the 2,249 cancers to which death was attributed, 1,780 (79%) were microscopically proved, 381 were not microscopically proved, and 88 may or may not have been microscopically proved (i. e., information from death certificate only).

The general findings for cancer are shown in tables 4, 5, and 6. The following statements can be made for the microscopically proved cases as well as for the total group: 1. In every age group, the death rates of the men with a history of regular cigarette smoking were higher than the death rates of men who never smoked. 2. The mortality ratio increased with the number of cigarettes smoked per day. 3. The death rates for pipe and cigar smokers were higher, on the average, than the death rates for men who never smoked.

Considering only microscopically proved cases, the mortality ratio was 1.92 for all men with a history of regular cigarette smoking. For men with a history of regular cigarette smoking only, the mortality ratio rose from 1.67 for smokers of under one-half pack of cigarettes a day to 1.82 for smokers of one-half to one pack a day, to 2.86 for smokers of one to two packs a day, and to 3.31 for smokers of two packs or more a day. Both for all cases and for microscopically proved cases, the mortality ratios in the last two years of the study (November, 1953, through October, 1955) were in close agreement with the mortality ratios in the earlier part of the study (January, 1952, through October, 1953).

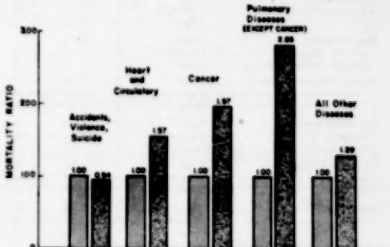

Fig. 1.—Mortality ratios by major causes of death. Ratios for cigarette smokers are compared with those for men who never smoked.

The deaths due to cancer were divided into six groups (see fig. 2) by primary site (plus a seventh group, primary site unknown). Of those with primary site specified, by far the highest association with cigarette smoking was found in primary cancer of the lung, the next highest group being the following sites combined: lip, tongue, floor of mouth, pharynx, larynx, and esophagus. Considering microscopically proved cancer of all specified primary sites other than those just mentioned, the mortality ratio for men with a history of regular cigarette smoking was 1.28, and the mortality ratio for smokers of one pack or more a day was 1.61.

Lung Cancer.—Primary cancer of the lung was recorded as the cause of 448 deaths. Only 15 of these men had never smoked, and 8 had smoked only occasionally. Three hundred ninety-seven deaths attributed to lung cancer occurred among men with a history of regular cigarette smoking, as compared with 37 expected deaths, giving a mortality ratio of 10.73. Only 18 of these deaths occurred among men who smoked pipes only and 7 among men who smoked cigars only. Among men with a history of cigarette smoking only, the death rate increased rapidly with current amount of smoking.

TABLE 4.—*Number of Cancer Deaths and Death Rates Per 100,000 Man-Years by Age at Start of Study for Men Divided into Three Groups by Smoking History**

Primary Site of Cancer	Smoking History	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected† No. of Deaths Observed	Expected	Ratio
Total: cancer	None	35	105	65	197	67	241	91	416	258	...	1.00
(with or without	Cigarette	226	189	430	358	428	567	326	804	1,460	741	1.97
microscopic proof)	Other	42	104	112	242	161	502	216	566	531	460	1.83
Lung	None	1	3	3	9	2	7	9	41	15	...	1.00
	Cigarette	83	57	141	117	108	136	70	173	397	37	10.73
	Other	4	10	11	24	8	18	13	34	36	24	1.50
Lip, tongue,	None	1	3	2	6	1	4	2	9	6	...	1.00
mouth, pharynx,	Cigarette	16	11	26	22	28	37	21	52	91	18	5.06
larynx, esophagus	Other	3	7	7	15	9	20	11	29	30	9	3.33
Genitourinary system	None	3	9	7	21	14	50	25	114	49	...	1.00
	Cigarette	32	22	47	39	69	91	70	173	218	123	1.77
	Other	4	10	13	28	42	94	52	136	111	80	1.39
Digestive system	None	16	48	33	100	32	115	36	164	117	...	1.00
(except	Cigarette	85	58	124	103	142	188	115	284	466	344	1.35
esophagus)	Other	15	37	53	114	80	180	97	254	245	180	1.36
Lymphatic and	None	7	21	8	24	13	47	8	37	36	...	1.00
hematopoietic	Cigarette	30	21	44	37	35	46	26	64	135	110	1.23
system	Other	8	20	13	28	12	27	23	60	56	55	1.02
Other specific sites	None	6	18	12	37	4	14	6	27	28	...	1.00
	Cigarette	18	12	36	30	25	33	12	30	91	92	0.99
	Other	7	17	13	28	13	29	10	28	43	41	1.05
Unknown primary site	None	1	3	0	0	1	4	5	23	7	...	1.00
	Cigarette	12	8	12	10	26	34	12	30	62	16	3.88
	Other	1	3	2	4	7	16	10	28	20	12	1.67
Total: cancer	None	28	84	56	170	55	198	69	315	208	...	1.00
(with microscopic	Cigarette	225	154	393	302	348	461	224	553	1,160	605	1.92
proof)	Other	33	81	98	211	131	294	150	393	412	321	1.28
Bronchogenic	None	0	0	1	3	0	0	3	14	4	...	1.00
(except	Cigarette	61	42	102	85	79	105	37	91	279	9	31.00
adenocarcinoma)	Other	3	7	9	19	6	14	8	21	26	7	3.71
Bronchogenic,	None	1	3	0	0	0	0	1	5	2	...	1.00
adenocarcinoma	Cigarette	7	5	13	11	4	5	2	5	26	6	4.33
	Other	0	0	2	4	1	2	1	3	4	3	1.33
Lip, tongue,	None	1	3	1	3	0	0	2	9	4	...	1.00
mouth, pharynx,	Cigarette	16	11	23	19	25	33	20	49	84	12	7.00
larynx, esophagus	Other	3	7	6	13	9	20	8	21	26	6	4.33
Genitourinary system	None	1	3	7	21	9	32	21	98	38	...	1.00
	Cigarette	25	17	37	31	59	78	56	138	177	93	1.90
	Other	4	10	11	24	22	49	35	92	72	62	1.16
Digestive system	None	14	42	28	85	29	104	29	133	100	...	1.00
(except	Cigarette	70	48	108	90	113	150	74	185	365	296	1.23
esophagus)	Other	9	22	44	95	66	148	65	170	184	154	1.19
Lymphatic and	None	5	15	8	24	11	40	7	32	31	...	1.00
hematopoietic	Cigarette	24	16	39	33	30	40	29	49	113	94	1.20
system	Other	7	17	12	26	9	20	20	52	48	47	1.02
Other specific sites	None	6	18	11	33	5	18	5	23	27	...	1.00
	Cigarette	15	10	33	28	22	29	9	22	79	80	0.99
	Other	6	15	12	30	12	27	9	24	39	40	0.98
Unknown primary site	None	0	0	0	0	1	4	1	5	2	...	1.00
	Cigarette	7	5	8	7	16	21	6	15	37	5	7.40
	Other	1	3	2	4	6	14	4	11	13	3	4.33

* "None" refers to no history of smoking; "cigarette" refers to regular smoking of cigarettes (including additional cigar or pipe smoking); and "other" refers to occasional smoking, cigar smoking, and pipe smoking but no regular cigarette smoking.

† Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of men in each of the other groups.

TABLE 5.—*Number of Cancer Deaths and Death Rates Per 100,000 Man-Years by Age at Start of Study for Men with History of Regular Cigarette Smoking Only*

Primary Site of Cancer	Packs Per Day	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Total: cancer (with or	**<½**	**20**	**213**	**33**	**392**	**27**	**474**	**23**	**638**	**103**	**55**	**1.87**
without microscopic	**½-1**	**74**	**180**	**113**	**385**	**79**	**471**	**66**	**821**	**332**	**173**	**1.92**
proof)	**1+**	**71**	**238**	**105**	**502**	**85**	**929**	**51**	**1,358**	**312**	**106**	**2.94**
Lung	**<½**	**6**	**64**	**6**	**71**	**5**	**88**	**7**	**191**	**24**	**3**	**8.00**
	½-1	**16**	**41**	**35**	**119**	**15**	**90**	**18**	**224**	**84**	**8**	**10.50**
	1+	**39**	**100**	**45**	**241**	**29**	**317**	**13**	**346**	**117**	**5**	**23.40**
Lip, tongue,	**<½**	**2**	**21**	**1**	**12**	**2**	**35**	**2**	**55**	**7**	**1**	**7.00**
mouth, pharynx,	**½-1**	**4**	**10**	**6**	**27**	**7**	**42**	**5**	**62**	**24**	**4**	**6.00**
larynx, esophagus	**1+**	**3**	**10**	**7**	**37**	**5**	**55**	**8**	**213**	**23**	**3**	**7.67**
Genitourinary	**<½**	**4**	**43**	**5**	**59**	**5**	**86**	**5**	**137**	**19**	**10**	**1.90**
system	**½-1**	**7**	**18**	**14**	**48**	**14**	**84**	**14**	**174**	**49**	**27**	**1.81**
	+1	**10**	**33**	**12**	**64**	**14**	**153**	**11**	**293**	**47**	**16**	**2.94**
Digestive system	**<½**	**6**	**64**	**10**	**119**	**8**	**140**	**7**	**191**	**31**	**26**	**1.19**
(except	**½-1**	**28**	**71**	**32**	**109**	**17**	**101**	**24**	**290**	**101**	**81**	**1.25**
esophagus)	**1+**	**14**	**47**	**19**	**102**	**25**	**273**	**13**	**346**	**71**	**50**	**1.42**
Lymphatic and	**<½**	**2**	**21**	**6**	**71**	**2**	**35**	**1**	**27**	**11**	**8**	**1.38**
hematopoietic	**½-1**	**9**	**23**	**10**	**34**	**9**	**54**	**3**	**37**	**31**	**26**	**1.19**
system	**1+**	**9**	**30**	**12**	**64**	**4**	**44**	**1**	**27**	**26**	**17**	**1.53**
Other specific	**<½**	**0**	**0**	**0**	**0**	**2**	**35**	**0**	**0**	**5**	**7**	**0.71**
sites	**½-1**	**5**	**13**	**10**	**34**	**4**	**48**	**1**	**12**	**24**	**22**	**1.09**
	1+	**1**	**3**	**10**	**54**	**4**	**44**	**3**	**80**	**18**	**15**	**1.20**
Unknown primary	**<½**	**0**	**0**	**2**	**24**	**3**	**53**	**1**	**27**	**6**	**1**	**6.00**
site	**½-1**	**5**	**13**	**4**	**14**	**9**	**54**	**1**	**15**	**19**	**4**	**4.75**
	1+	**4**	**13**	**0**	**0**	**4**	**44**	**2**	**53**	**10**	**2**	**5.00**
Total: cancer	**<½**	**16**	**170**	**25**	**297**	**20**	**351**	**14**	**382**	**75**	**45**	**1.67**
(with microscopic	**½-1**	**53**	**135**	**96**	**327**	**65**	**388**	**45**	**560**	**230**	**142**	**1.62**
proof)	**1+**	**61**	**204**	**87**	**465**	**71**	**776**	**37**	**985**	**256**	**87**	**2.94**
Bronchogenic	**<½**	**3**	**32**	**4**	**47**	**2**	**35**	**4**	**100**	**13**	**<1**	**16.25**
(except	**½-1**	**11**	**29**	**22**	**75**	**10**	**60**	**8**	**160**	**51**	**2**	**25.50**
adenocarcinoma)	**1+**	**24**	**80**	**33**	**177**	**24**	**262**	**7**	**186**	**88**	**1**	**88.00**
Bronchogenic,	**<½**	**0**	**0**	**1**	**12**	**0**	**0**	**0**	**0**	**1**	**<1**	**2.00**
adenocarcinoma	**½-1**	**0**	**0**	**4**	**14**	**1**	**6**	**0**	**0**	**5**	**2**	**2.50**
	1+	**4**	**13**	**2**	**11**	**1**	**11**	**0**	**0**	**7**	**1**	**7.00**
Lip, tongue,	**<½**	**2**	**21**	**1**	**12**	**2**	**35**	**2**	**55**	**7**	**<1**	**7.78**
mouth, pharynx,	**½-1**	**4**	**10**	**6**	**20**	**6**	**36**	**5**	**62**	**21**	**3**	**7.00**
larynx, esophagus	**1+**	**3**	**10**	**6**	**32**	**4**	**44**	**8**	**213**	**21**	**2**	**10.50**
Genitourinary	**<½**	**4**	**43**	**3**	**36**	**4**	**70**	**3**	**82**	**14**	**7**	**2.00**
system	**½-1**	**5**	**13**	**12**	**41**	**14**	**84**	**11**	**137**	**42**	**21**	**2.00**
	1+	**7**	**23**	**11**	**59**	**14**	**158**	**9**	**240**	**41**	**12**	**3.42**
Digestive system	**<½**	**6**	**64**	**8**	**95**	**7**	**123**	**4**	**109**	**25**	**22**	**1.14**
(except	**½-1**	**21**	**54**	**30**	**102**	**12**	**72**	**17**	**232**	**80**	**70**	**1.14**
esophagus)	**1+**	**12**	**40**	**17**	**91**	**19**	**208**	**10**	**306**	**58**	**43**	**1.35**
Lymphatic and	**<½**	**1**	**11**	**5**	**59**	**2**	**35**	**0**	**0**	**8**	**7**	**1.14**
hematopoietic	**½-1**	**6**	**15**	**10**	**34**	**8**	**48**	**2**	**25**	**26**	**22**	**1.18**
system	**1+**	**7**	**23**	**9**	**48**	**4**	**44**	**1**	**27**	**21**	**14**	**1.50**
Other specific	**<½**	**0**	**0**	**2**	**24**	**2**	**35**	**0**	**0**	**4**	**6**	**0.67**
sites	**½-1**	**4**	**10**	**9**	**31**	**7**	**42**	**1**	**12**	**21**	**22**	**0.95**
	1+	**1**	**3**	**9**	**48**	**3**	**53**	**1**	**27**	**14**	**14**	**1.00**
Unknown primary	**<½**	**0**	**0**	**1**	**12**	**1**	**18**	**1**	**27**	**3**	**<1**	**7.50**
site	**½-1**	**2**	**5**	**3**	**10**	**7**	**42**	**1**	**12**	**13**	**1**	**13.00**
	1+	**3**	**10**	**0**	**0**	**2**	**22**	**1**	**27**	**6**	**<1**	**12.00**

* Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of men in each of the other groups.

TABLE 6.—*Observed Versus Expected* Number of Cancer Deaths by Primary Site for Men with History of Occasional Smoking Only, Pipe Smoking Only, and Cigar Smoking Only*

Primary Site of Cancer	Occasional Only Observed	Occasional Only Expected	Occasional Only Ratio	Pipe Only Observed	Pipe Only Expected	Pipe Only Ratio	Cigar Only Observed	Cigar Only Expected	Cigar Only Ratio
Total: cancer (with or without microscopic proof)	**115**	**93**	**1.24**	**155**	**108**	**1.44**	**160**	**119**	**1.34**
Lung	**8**	**6**	**1.33**	**18**	**7**	**2.57**	**7**	**7**	**1.00**
Lip, tongue, mouth, pharynx, larynx, esophagus	**3**	**2**	**1.50**	**9**	**3**	**3.00**	**11**	**3**	**3.67**
Genitourinary system	**26**	**18**	**1.44**	**31**	**22**	**1.41**	**27**	**23**	**1.17**
Digestive system (except esophagus)	**49**	**42**	**1.17**	**61**	**48**	**1.27**	**80**	**54**	**1.48**
Lymphatic and hematopoietic system	**19**	**13**	**1.46**	**17**	**14**	**1.21**	**11**	**16**	**0.69**
Other specified sites	**5**	**10**	**0.50**	**16**	**10**	**1.60**	**13**	**13**	**1.00**
Unknown primary site	**5**	**3**	**1.67**	**3**	**3**	**1.00**	**11**	**3**	**3.67**
Total: cancer (with microscopic proof)	**85**	**75**	**1.13**	**115**	**86**	**1.34**	**129**	**96**	**1.34**
Bronchogenic (except adenocarcinoma)	**5**	**2**	**2.50**	**13**	**2**	**6.50**	**6**	**2**	**3.00**
Bronchogenic, adenocarcinoma	**1**	**<1**	**1.43**	**2**	**<1**	**2.50**	**1**	**<1**	**1.11**
Lip, tongue, mouth, pharynx, Larynx, esophagus	**3**	**1**	**3.00**	**7**	**2**	**3.50**	**10**	**2**	**5.00**
Genitourinary system	**19**	**14**	**1.36**	**21**	**18**	**1.17**	**19**	**18**	**1.06**
Digestive system (except esophagus)	**35**	**36**	**0.97**	**41**	**41**	**1.00**	**63**	**46**	**1.37**
Lymphatic and hematopoietic system	**15**	**11**	**1.36**	**15**	**12**	**1.25**	**10**	**14**	**0.71**
Other specified sites	**5**	**10**	**0.50**	**14**	**10**	**1.40**	**12**	**12**	**1.00**
Unknown primary site	**2**	**<1**	**2.86**	**2**	**1**	**2.00**	**8**	**1**	**8.00**

* Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of men in each of the other groups.

The 448 cases were further classified as follows: 309 microscopically proved cases of bronchogenic carcinomas other than adenocarcinoma, 32 microscopically proved bronchogenic adenocarcinomas,

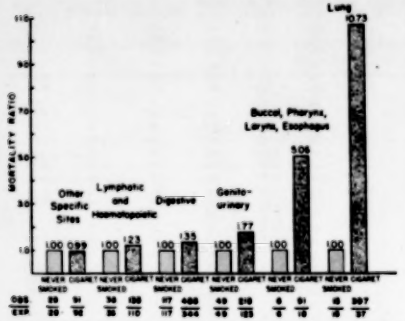

Fig. 2.—Mortality ratios by sites of cancer. Ratios for cigarette smokers are compared with those for men who never smoked.

1 myxofibrosarcoma, 93 cases in which diagnosis was based on x-ray or clinical evidence only, and 13 cases in which the disease may or may not have been microscopically proved (i. e., information from death certificate only).

Adenocarcinoma of the bronchus is considered separately because some investigators [3] have suggested that this form of lung cancer may be less

TABLE 7.—*Number of Deaths and Age-Standardized Death Rates* from Lung Cancer by Smoking Habits*

Smoking Habits	All Cases		Well-Established Cases (Excluding Adenocarcinoma)		Adenocarcinoma	
	No. of Deaths	Death Rate	No. of Deaths	Death Rate	No. of Deaths	Death Rate
Never smoked	15	12.8	4	3.4	2	1.8
Occasional only	8	19.2	5	11.9	1	2.3
Cigars only	7	13.1	6	11.4	1	1.7
Pipes only	18	38.5	13	28.9	2	4.4
Cigars and pipes	3	7.3	2	4.9	0	...
Cigarettes and other	148	97.7	108	67.0	12	7.3
Cigarettes only	249	127.2	162	78.6	14	6.1
Total	448	68.0	295	44.5	32	4.7
Current daily cigarette smoking†						
<½ pack	21	95.2	13	51.4	1	3.3
½-1 pack	84	107.8	50	59.3	5	5.1
1-2 packs	90	229.2	60	143.9	7	11.6
2+ packs	27	304.2	22	217.3	0	...

* Death rate per 100,000 man-years standardized to the age distribution of the white male population of the United States as of July, 1954.

† History of cigarette smoking only.

associated with smoking than are other forms. The findings, as shown in tables 4, 5, and 6, are consistent with this theory, but with only 32 cases we cannot be sure. Nevertheless, this form of bronchogenic carcinoma was highly associated with cigarette smoking. Twenty-six of the 32 deaths occurred among men with a history of regular cigarette smoking, as compared with only six expected deaths. The difference of 20 deaths is statistically significant ($p=0.05$).

Of the 309 microscopically proved cases (other than adenocarcinoma), 295 were well established as being bronchogenic in origin. The diagnosis in the other 14 was less certain (e. g., diagnosis based on clinical and x-ray findings in the lung with cancer proved by biopsy of a metastatic site). These 14 uncertain cases, in all of which the patients were cigarette smokers, have been excluded from the group which will hereafter be described as well-established cases of bronchogenic carcinoma, excluding adenocarcinoma.

Only four men who never smoked died of well-established bronchogenic carcinoma (excluding adenocarcinoma). Since this is a small number to use as a basis for mortality ratios, we summarized

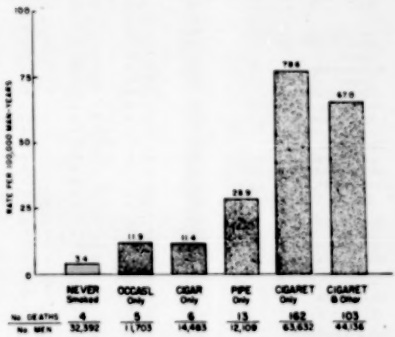

Fig. 3.—Age-standardized death rates due to well-established cases of bronchogenic carcinoma (exclusive of adenocarcinoma) by type of smoking as classified from lifetime history.

the findings, as shown in table 7, by computing death rates standardized to the age distribution of the white male population of the United States in 1954. Figure 3 shows the age-standardized death rates for well-established cases by type of smoking (classified from lifetime history). The numbers at the bottom of this figure indicate the corresponding number of men who were enrolled in 1952. The rates were low for men who never smoked, occasional smokers, and cigar smokers. Pipe smokers had an appreciably higher rate. The rate for men with a history of regular cigarette smoking only was 23 times as high as the rate for men who never smoked.

Figure 4 shows the rates for men with well-established cases (excluding adenocarcinoma) by amount of cigarette smoking for men with a history

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of regular cigarette smoking only. The rates increased rapidly with amount of cigarette smoking. The age-standardized death rate for smokers of two or more packs a day was 217.3 per 100,000 per year. In contrast, the age-standardized death rate from microscopically proved cancer, all sites combined, was only 177.4 per 100,000 per year for men who never smoked. In other words, among smokers of two packs of cigarettes a day, the death rate from bronchogenic carcinoma alone is higher than the total death rate due to cancer of men who never smoked.

As shown in figure 4, rates for men who had given up cigarette smoking were lower than the rates for men who were smoking cigarettes regularly at the time of questioning in 1952. Figure 5 shows the age-standardized death rates (well-established cases excluding adenocarcinoma) for men with a history of regular cigarette smoking only, who had stopped smoking cigarettes in 1952,

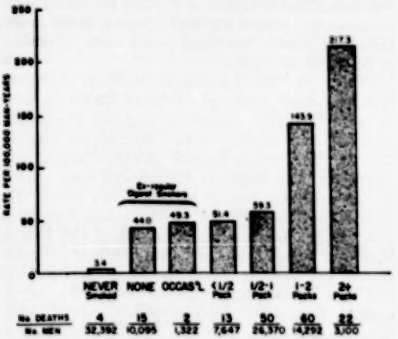

Fig. 4.—Age-standardized death rates due to well-established cases of bronchogenic carcinoma (exclusive of adenocarcinoma) by current amount of cigarette smoking.

by previous daily consumption of cigarettes and by number of years since they had last smoked. The rate for men currently smoking less than one pack of cigarettes a day in 1952 was 57.6 per 100,000 per year. Those who had previously smoked at this level but had given up smoking for from 1 to 10 years was 35.5, and the rate for those who had given up smoking for 10 years or longer was only 8.3. The rate for men currently smoking one pack or more of cigarettes a day in 1952 was 157.1 per 100,000 per year. Those who had previously smoked at that level but had given up smoking for from 1 to 10 years was 77.6, and the rate for those who had given up smoking for 10 years or longer was 60.5.

The number of years of cigarette smoking, as well as the amount of smoking, seems to be of importance. The following figures include all deaths from lung cancer. For men with a history of regular cigarette smoking only who were smoking less than one-half pack a day in 1952, the age-standardized death rate was 68 per 100,000 per year for those

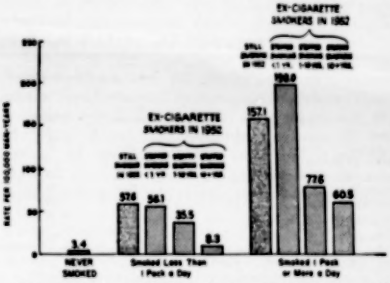

Fig. 5.—Age-standardized death rates due to well-established cases of bronchogenic carcinoma (exclusive of adenocarcinoma). Rates for men who have stopped smoking are compared with those for men who never smoked and those for men still smoking in 1952.

who had smoked for less than 35 years and 139 for those who had smoked for 35 years or longer. Among smokers of one-half to one pack a day, the rates were 84 for those who had smoked for less than 35 years and 105 for those who had smoked for 35 years or longer. For smokers of one to two packs a day, the rates were 93 and 252 respectively. For smokers of two packs or more a day, the rates were 138 and 293 respectively.

As expected, the death rate due to lung cancer (well-established cases exclusive of adenocarcinoma) was found to be higher in urban than in rural areas (table 8). The age-standardized death rate was 34 per 100,000 in rural areas, as compared with 56 per 100,000 in cities of over 50,000 population.

TABLE 8.—*Rates of Death Due to Lung Cancer, by Urban-Rural Classification, Standardized for Age and for Age and Smoking Habits*

	Cities			
	50,000+	10,000-50,000	Towns	Rural
Men, no.	45,218	43,502	50,039	46,780
Cigarette smokers, %	62.5	60.1	56.9	50.4
Total lung cancer cases				
Death rate standardized for age	82	68	73	52
Death rate standardized for age and for smoking habits	75	66	73	59
Well-established* lung cancer cases				
Death rate standardized for age	56	46	43	34
Death rate standardized for age and for smoking habits	52	44	43	39

* Well-established cases of bronchogenic carcinoma, exclusive of adenocarcinoma.

However, cigarette smoking is more common among city dwellers than among men in rural areas. Standardized for smoking habits as well as for age, the rate was 39 per 100,000 in rural areas and 52 per 100,000 in cities of over 50,000 population. Thus,

when standardized for both factors, the rate was still 25% lower in rural areas than in large cities. This difference may be due to some factor producing lung cancer associated with city life or to better case finding and diagnosis in cities than in rural areas.

ratio was 18.00 in the first part of the study and 31.50 in the second part of the study. Corresponding figures for well-established cases exclusive of adenocarcinoma are too unstable to make such a comparison, because of the small number of deaths due to this disease among men who never smoked.

TABLE 9.—*Number of Deaths from Cancer of Several Selected Sites by Smoking Habits*

Site of Cancer	Total No. of Deaths	Microscopically Proved Cases						
			Type of Smoking					
		Total	Never Smoked	Occasional Only	Cigarette Only	Pipe Only	Cigar Only	Other*
Lip	1	1	0	0	1	0	0	0
Tongue	17	16	1	1	2	4	0	8
Floor of mouth	6	6	0	0	5	0	1	0
Other part of mouth	8	8	0	1	0	0	3	4
Pharynx	27	25	2	0	12	1	1	9
Larynx	36	34	0	0	17	0	3	4
Esophagus	42	34	1	1	15	2	2	13
Total	127	114	4	3	52	7	10	38

* Two or three types of smoking.

The rate of deaths due to lung cancer was low among men who never smoked cigarettes regularly and high among cigarette smokers in large cities, small cities, suburbs and towns, and rural areas (fig. 6). Whatever the urban factor may be, its effect on these rates is small as compared with the effect of cigarettes, as shown by the relative heights of the bars on this chart.

A comparison was made between the findings in the first part of the study (January, 1952, through October, 1953) with the findings in the last two years of the study (November, 1953, through October, 1955). Considering all deaths reported as due to lung cancer, the mortality ratio of men with a history of regular cigarette smoking only was 9.64 in the first part of the study and 14.30 in the second part of the study. For men with a history of regular cigarette smoking only who were currently smoking one pack or more a day, the mortality

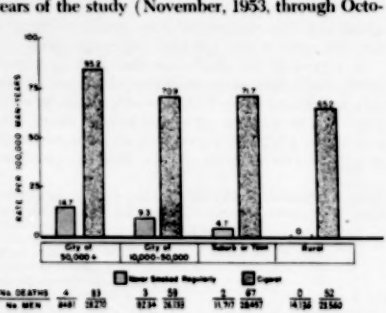

Fig. 6.—Age-standardized death rates due to well-established cases of bronchogenic carcinoma (exclusive of adenocarcinoma) by urban-rural classification. Rates for cigarette smokers are compared with those for men who never smoked regularly.

However, the rate of deaths due to lung cancer was considerably higher in the last two years than in the earlier part of the study. Trends in the death rates and reasons for these trends were discussed in part 1 of this paper.

Cancer of the Esophagus, Larynx, Pharynx, Mouth, Tongue, and Lip.—Tobacco smoke (or saliva and bronchial secretions containing material from tobacco smoke) comes into direct contact with the lips, mouth, tongue, pharynx, larynx, and esophagus. The deaths of 127 subjects were attributed to primary cancer of these sites (table 9). Only six of these men had never smoked, and three were occasional smokers. The other 118 had a history of regular smoking. One hundred fourteen of the 127 cancers were microscopically proved and only 4 of these were in men who never smoked. Considering microscopically proved cases only, the mortality ratio was 7.00 for men with a history of regular cigarette smoking (many of whom smoked pipes and cigars as well as cigarettes), 5.00 for men who smoked only cigars, and 3.50 for men who smoked only pipes. Still considering microscopically proved cases, 52 men had a history of regular cigarette smoking only, 7 had a history of regular pipe smoking only, 10 had a history of regular cigar smoking only, and 38 had a history of two or three types of smoking. The figures suggest that pipe and cigar smoking may be more important than cigarette smoking in relation to cancer of one or more of the sites included in this group, but the number of cases is not sufficient for a reliable evaluation of this point.

Considering microscopically proved cases, out of 34 deaths from cancer of the esophagus only 1 was of a man who had never smoked, of 25 deaths from cancer of the pharynx only 2 were of men who had never smoked, and of 16 deaths from cancer of the tongue only 1 was of a man who had never smoked. No deaths of men who never smoked

were reported among 24 cases of cancer of the larynx, 14 cases of cancer of the mouth, and 1 case of cancer of the lip.

Cancer of the Genitourinary System.—Tables 4, 5, and 6 show a summary of the findings for the 368 deaths from cancer of the genitourinary system, 287 of which cases were microscopically proved. The mortality ratios for men with a history of regular cigarette smoking were 1.77 for all cases and 1.90 for microscopically proved cases. For smokers of one pack or more a day of cigarettes, the mortality ratios were 2.94 for all cases and 3.42 for microscopically proved cases. These ratios are significantly greater than 1.00 ($p < 0.001$ in both instances).

Of these 368 cases, 106 apparently originated in the bladder, 67 in the kidney, 185 in the prostate, and 10 in other parts of the genitourinary system (table 10). We say "apparently" because in many of these cases the tumor involved two or more of these organs, as well as other nearby structures, and the doctor sometimes expressed doubt as to the exact location of the primary lesion.

Among men with a history of regular cigarette smoking, there were 59 deaths from microscopically proved cases of cancer of the bladder, as compared with 27 expected deaths, a difference of 32 deaths and a mortality ratio of 2.17. This difference is statistically significant ($p=0.02$). In cases of microscopically proved cancer of the prostate, there were 77 deaths among cigarette smokers, compared with 44 expected deaths (mortality ratio, 1.75), and this difference is statistically significant ($p=0.05$). In cases of microscopically proved cancer of the kidney, there were 35 deaths among cigarette smokers, compared with 22 expected deaths (mortality ratio, 1.58); this difference is not statistically significant ($p=0.30$).

Cancer of the Digestive System.—There were 828 deaths attributed to cancer of the digestive system (exclusive of the 42 cases of cancer of the esophagus), of which 649 cases were microscopically proved. The mortality ratio for men with a history of regular cigarette smoking was 1.35 for all men but 1.23 for men with microscopically proved cases. The sites to which the 828 cases were ascribed were stomach, 240; pancreas, 150; liver, gallbladder, and biliary passages, 70; colon, 226; rectum, 119; and other and uncertain sites in the digestive system, 23 (table 10).

The most striking association with cigarette smoking was for deaths ascribed to cancer of the liver, the mortality ratio being 4.52 for men with microscopically proved cases. The liver is one of the most frequent sites of metastases, and in many if not most of these cases there was doubt as to the primary site.

There was a negative association between cigarette smoking and deaths ascribed to cancer of the colon (mortality ratio, 0.77), but this was not statistically significant ($p=0.43$). There was no association between cigarette smoking and cancer of the rectum. The mortality ratio of cigarette smokers was 1.61 for men with cancer of the stomach and 1.50 for men with cancer of the pancreas. In neither case was the difference between observed and expected deaths statistically significant ($p=0.12$ and $p=0.10$ respectively).

Cancer of the Lymphatic and Hematopoietic System.—There were 227 deaths ascribed to cancer of the lymphatic and hematopoietic system. These included lymphosarcoma and reticulosarcoma, 66; Hodgkin's disease, 30; multiple myeloma, 32; leukemia, 88; and other, 11 (table 10). Leukemia showed no indication of an association with cigarette smoking. Hodgkin's disease, as well as lympho-

TABLE 10.—*Number of Deaths and Observed Versus Expected* Deaths for Men with History of Regular Cigarette Smoking by Primary Sites of Cancer of Genitourinary, Digestive, and Lymphatic and Hematopoietic Systems*

Site of Cancer	Total No. of Deaths	Microscopically Proved Cases			
		Observed Vs. Expected No. of Deaths			
		Total	Observed	Expected	Ratio
Genitourinary system	368	287	177	93.4	1.90
Bladder	106	90	59	27.2	2.17
Kidney	67	54	35	22.1	1.58
Prostate	185	134	77	44.1	1.75
Other	10	9	6	0	...
Digestive system	828	649	365	296.2	1.23
Stomach	240	176	107	66.5	1.61
Pancreas	150	117	76	50.5	1.50
Liver, gallbladder, and biliary passages	70	47	33	7.3	4.52
Colon	226	168	84	108.4	0.77
Rectum	119	104	55	58.8	0.94
Other	23	12	10	4.4	...
Lymphatic and hematopoietic system	227	192	113	93.9	1.20
Lymphosarcoma and reticulosarcoma	66	57	36	20.8	1.73
Hodgkin's disease	30	25	20	7.3	2.74
Multiple myeloma	32	28	12	18.2	0.66
Leukemia	88	73	39	46.0	0.85
Other	11	9	6	1.9	...

* Calculated by applying the age-specific death rates of men who never smoked to the man-years of exposure to risk of the men with a history of regular cigarette smoking.

sarcoma and reticulosarcoma, appeared to be associated with cigarette smoking, but in neither was the difference between observed and expected deaths statistically significant. For multiple myeloma, the observed number of deaths among cigarette smokers was smaller than the expected number (12 versus 18), but with so few cases, this difference is not statistically significant.

Cancer of Other Sites.—There were 162 deaths from cancer of other specified sites, of which 145 were of patients with microscopically proved cases. Taken as a group, these showed no association with cigarette smoking. The 162 cases consisted of brain, 74; pleura, 6; salivary gland, 9; other respiratory diseases, 7; melanoma, 17; skin, 9; eye, 2; thyroid, 5; bone, 13; adrenal, 4; breast, 5; connec-

tive tissue, 5; and other sites, 6. None of these showed a statistically significant degree of association with cigarette smoking habits.

Primary site could not be determined in 89 cases, 52 of which were microscopically proved cancer. These deaths showed a high degree of association with smoking habits.

Heart and Circulatory Diseases

Of the 11,870 deaths in the study, 7,523 (63%) were attributed to diseases of the heart and circulatory system (including vascular lesions of the central nervous system). The International Statistical Classification of Diseases, Injuries, and Causes of Death, Sixth Revision, makes provision for distinguishing between 47 specific disease entities in these general categories (including some rather vaguely described conditions). The only difficulty is that in many instances in this study two or more of these diseases were present and apparently contributed to death.

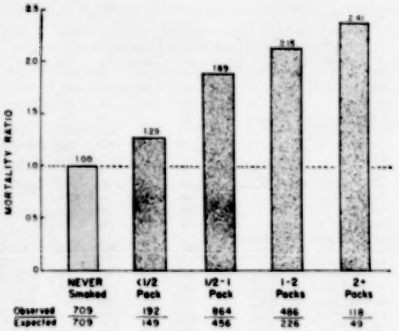

Fig. 7.—Mortality ratios due to coronary artery disease by current amount of cigarette smoking.

Cerebral vascular lesions were recorded as a contributing factor in 135 (36.2%) of the 373 deaths attributed primarily to hypertensive heart disease and in 140 (2.6%) of the 5,297 deaths attributed primarily to coronary artery disease. Coronary artery disease was recorded as a contributing factor in 51 (4.9%) of the 1,050 deaths ascribed to cerebral vascular lesions and 79 (6.7%) of the deaths ascribed primarily to other heart and circulatory diseases. All told, cerebral vascular lesions were recorded in 408 deaths attributed primarily to some other cause, and coronary artery disease was recorded in 384 deaths attributed to some other cause. We attempted to analyze the data for each of the many combinations, but this turned out to be fruitless. Therefore, we turned to the usual procedure of classifying each death according to the presumed principal underlying cause, regardless of how many other conditions were mentioned.

First, we divided the 7,523 deaths due to heart and circulatory diseases into four groups: coronary artery disease (5,297 deaths), other heart diseases (911 deaths), cerebral vascular lesions (1,050 deaths), and other circulatory diseases (265 deaths). The figures for these are shown on tables 1, 2, and 3. Coronary artery disease and "other circulatory diseases" showed a high degree of association with cigarette smoking; cerebral vascular lesions showed a moderate degree of association with cigarette smoking; and other heart diseases showed a small degree of association with cigarette smoking.

Coronary Artery Disease.—Coronary artery disease is of particular importance, because it accounts for a large proportion of all deaths in the United States, the highest rates being among men in the older age groups. In this study, it accounted for 44.6% of all deaths. Therefore, even a moderate percentage increase in deaths from this cause has an appreciable effect on the total death rate.

In all four age groups the death rates from coronary artery disease were far higher among men with a history of regular cigarette smoking than among men who never smoked (see table 1). There were 3,361 deaths from this cause among the cigarette smokers, whereas only 1,973 would have died if their age-specific death rates had been the same as for men who never smoked ($p < 0.001$). As shown by the mortality ratio of 1.70, the death rate from this cause of these cigarette smokers was 70% higher than for a comparable group of men who never smoked. Death rates due to coronary artery disease increased with the amount of cigarette smoking. Among men with a history of regular cigarette smoking only, the mortality ratio rose from 1.29 for men smoking less than one-half pack of cigarettes a day to 1.89 for smokers of one-half to one pack a day, to 2.15 for smokers of one to two packs a day, and to 2.41 for smokers of two packs or more a day (fig. 7).

Men with a history of cigar smoking only also had higher death rates from coronary artery diseases than men who never smoked (observed deaths, 420, expected deaths, 329, ratio, 1.28). This difference is statistically significant ($p < 0.001$). The rates for pipe smokers were about the same as for men who never smoked.

The degree of association with cigarette smoking was higher for deaths specifically described as due to arteriosclerotic heart disease than for deaths described as due to coronary thrombosis, embolism, or occlusion or to myocardial infarction.

Figure 8 shows mortality ratios for men with a history of regular cigarette smoking only, comparing those for men who had stopped smoking with those for men who were smoking regularly in 1952.

The mortality ratios of men who had given up smoking for 10 years or longer were much less than those for men who continued to smoke, amount being taken into consideration. The mortality ratios of men who had given up smoking for less than a year were higher than the corresponding ratios for men who were still smoking in 1952. The high ratios for those who had stopped smoking for less than a year may have been due to the inclusion in this group of some men who had recently stopped smoking because of symptoms of heart disease.

The association between cigarette smoking and death rates due to coronary artery disease was about the same in the last two years of the study (November, 1953, through October, 1955) as in the earlier part of the study (January, 1952, through October, 1953). For example, comparing all men with a history of regular cigarette smoking to men who never smoked, the mortality ratio was 1.74 in the first part of the study and 1.68 in the second part of the study. The difference between these two ratios is not statistically significant. The mortality ratio for men with a history of regular cigarette smoking only who smoked one pack or more of cigarettes a day was 2.09 in the first part of the study and 2.27 in the second part of the study.

Other Heart Diseases.—Other heart diseases accounted for 911 (7.7%) of the 11,870 deaths in the study. This group consisted of 167 deaths from chronic rheumatic heart disease, 373 from hypertensive heart disease, and 371 from miscellaneous other heart diseases, including many which were described in vague or nonspecific terms. Chronic rheumatic heart disease showed no association with cigarette smoking (mortality ratio 0.98). Hypertensive heart disease showed only a slight degree of association with cigarette smoking (mortality ratio 1.13). This was not statistically significant ($p=0.26$).

The other deaths ascribed to heart disease showed a statistically significant degree of association with cigarette smoking (mortality ratio 1.39, $p=0.05$). Some of these cases were probably due to coronary artery disease or to some other circulatory disease. The evidence seems to indicate that coronary artery disease is the only important form of heart disease which is associated with smoking habits.

Cerebral Vascular Lesions.—Vascular lesions of the central nervous system were recorded as the underlying cause of 1,050 (8.8%) of the 11,870 deaths. A total of 556 deaths due to this group of diseases occurred among men with a history of regular cigarette smoking, as compared with 428 expected deaths (a difference of 128 deaths and a mortality ratio of 1.30). This difference is statistically significant ($p=0.01$). The death rate increased with the amount of cigarette smoking, the mortality ratio being 1.46 for men smoking one pack or more of cigarettes a day.

Of the 1,050 deaths in this category, 237 were attributed to cerebral thrombosis or embolism, 749 were attributed to cerebral hemorrhage, and 64 were attributed to other vascular lesions of the central nervous system. Cases described as cerebral thrombosis showed about the same degree of relationship to smoking habits as did cases described as cerebral hemorrhage.

Other Circulatory Diseases.—The 265 deaths classified in table 1 under "other circulatory diseases" consisted of 50 attributed to hypertensive disease without mention of heart, 39 attributed to phlebitis and embolism (international list numbers 463-468), 59 attributed to general arteriosclerosis, 90 attributed to aortic aneurysm (nonsyphilitic), and 27 attributed to miscellaneous other circulatory diseases, including aneurysms and thromboangiitis obliterans (5 cases). Hypertensive diseases showed no association with cigarette smoking (mortality ratio 1.00).

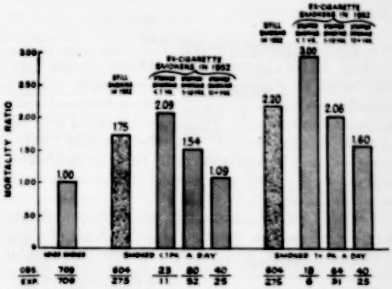

Fig. 8.—Mortality ratios due to coronary artery disease. Rates for men who have stopped smoking are compared with those for men who never smoked and those for men still smoking in 1952.

General arteriosclerosis and the group including phlebitis and embolism both showed a moderate degree of association with cigarette smoking. However, there were not many cases, and in neither disease was the association statistically significant.

Sixty-eight of the deaths from aortic aneurysm occurred among men with a history of regular cigarette smoking, compared with only 25 expected deaths. This difference of 43 deaths (mortality ratio 2.72) is statistically significant ($p=0.005$).

In the miscellaneous group (which included other aneurysms, gangrene, and thromboangiitis obliterans), 18 of the deaths occurred among men with a history of regular cigarette smoking, compared with only 4 expected deaths.

Pulmonary Diseases

Only 338 deaths were ascribed to pulmonary diseases other than lung cancer. Of these, 124 were attributed to pneumonia and influenza, 41 to pul-

monary tuberculosis, 76 to asthma, and 97 to other pulmonary diseases, including bronchitis, abscess of lung, pneumoconiosis, and bronchiectasis (international list numbers 500-502 and 520-527). A total of 231 deaths from all of these causes occurred among men with a history of regular cigarette smoking, compared with 81 expected deaths (a difference of 150 deaths and mortality ratio of 2.85). This difference is statistically significant ($p < 0.001$).

The mortality ratios for men with a history of regular cigarette smoking were as follows: for pneumonia and influenza, the mortality ratio was 3.90 and the difference between observed and expected deaths was statistically significant ($p < 0.001$); for asthma, the mortality ratio was 1.76, but it was not statistically significant ($p=0.08$); for pulmonary tuberculosis, the mortality ratio was 2.17, and this was not statistically significant ($p=0.24$); and for other pulmonary diseases, the mortality ratio was 3.62, and this was statistically significant ($p=0.005$).

Other Diseases

Only 1,120 (9.4%) of the 11,870 deaths were attributed to diseases other than cancer, cardiac, circulatory, and pulmonary diseases, and accidents, violence, and suicide. These were divided into 101 specific disease entities, plus the category "vague and unknown causes of death." Only three showed a statistically significant degree of association with smoking habits.

Gastric and Duodenal Ulcers.—Fifty-one deaths were attributed to gastric ulcers, and all of them occurred among men with a history of regular smoking. They were divided by smoking habits as follows: history of regular cigarette smoking only, 35; history of regular cigarette smoking and also regular pipe or cigar smoking, 11; history of pipe smoking only, 2; history of cigar smoking only, 2; and history of both pipe and cigar smoking but no cigarette smoking, 1. The death rate from gastric ulcer for men with a history of regular cigarette smoking only was about five times as high as the rate for cigar and pipe smokers who never smoked cigarettes regularly.

Gastric ulcers were recorded as a contributing factor in 33 deaths ascribed to some other cause (this in addition to the 51 cases described above). The mortality ratio for cigarette smokers was 3.46 in this group of cases ($p=0.08$).

Seventy-three deaths were attributed to duodenal ulcers. Fifty-four of them were of men with a history of regular cigarette smoking, compared with 25 expected deaths. This difference of 29 deaths (mortality ratio 2.16) is statistically significant ($p=0.05$).

Duodenal ulcers were listed as a contributing factor in 46 deaths ascribed to some other cause (this in addition to the 73 cases described above). The mortality ratio for cigarette smokers was 3.67 in this group of cases. This difference is statistically significant ($p=0.02$).

Cirrhosis of the Liver.—Of 127 deaths ascribed to cirrhosis of the liver, 83 occurred among men with a history of cigarette smoking, as compared with 43 expected deaths. This difference of 40 deaths (mortality ratio 1.93) is statistically significant ($p=0.05$).

Remainder of Diseases.—The remaining 869 deaths were attributed to 98 different specific diseases, plus the category "vague and unknown causes." Taking this entire group together, the death rate of the cigarette smokers was slightly higher than that of men who never smoked (mortality ratio 1.07) but the difference was not statistically significant. Diabetes, which accounted for 162 of these deaths, showed no association with smoking habits. No single one of the other 97 specific diseases showed a statistically significant association with smoking habits.

Comment

Other investigations have previously reported an association between smoking habits and many of the diseases for which we found the death rate to be higher among cigarette smokers than among nonsmokers. The literature on this subject is so extensive (particularly in relation to lung cancer) that it is impossible for us to review it in the space available here. However, we must mention that the findings on lung cancer reported by Doll and Hill [4] in their prospective study of British physicians were essentially the same as our findings.

We are fully aware of the fact that cause of death as recorded on death certificates is not always correct. Therefore, it is possible that some of the associations found between smoking habits and certain specific diseases may have resulted from errors in diagnosis. For example, it is conceivable that the association found between cigarette smoking and death ascribed to pulmonary tuberculosis may have resulted from confusion between tuberculosis and lung cancer. It is also conceivable that the relatively small association found between cigarette smoking and death from cerebral vascular lesions may have resulted from ascribing some deaths to this cause which were actually due to coronary artery disease.

In respect to cancer, we did not depend on death certificate information alone but obtained additional information from the doctor, hospital, or tumor registry. In 79% of the cases classified as cancer in this report, the diagnosis was microscopically confirmed. We found a high degree of association between cigarette smoking and microscopically proved cancer (all sites combined). It is extremely unlikely that this could have been produced by errors in diagnosis. It follows that there must be a high degree of association between cigarette smoking and cancer of one or more primary sites.

The next problem was to determine which specific site or sites of cancer are involved in this relationship. A difficulty arises from the fact that the primary site cannot always be established with certainty. The following relationships were found.

First, lung cancer showed an extremely high degree of association with cigarette smoking. The next highest association with cigarette smoking was for cancer of the following sites combined: lip, tongue, floor of mouth, pharynx, larynx, and esophagus. These are all sites directly exposed to cigarette smoke or material dissolved or condensed from cigarette smoke. Approximately 65% of the association between cigarette smoking and microscopically proved cancer (all sites combined) was accounted for by the association between cigarette smoking and cancer of the sites just mentioned. No site other than those just mentioned showed an extremely high degree of association with cigarette smoking (cancer of the liver being a possible exception).

Second, the degree of association between cigarette smoking and deaths attributed to lung cancer was higher for cancer microscopically proved and with good evidence as to the primary site than for the total group (including cancer not microscopically verified and cases with doubt as to primary site). The same was true for cancer of the genitourinary system.

Third, considering all deaths ascribed to cancer of the gastrointestinal system (except esophagus), there was only a small degree of association with cigarette smoking. In this group of cases, the association was lower for microscopically proved cases than for the total group. Furthermore, there was considerable doubt as to the primary site of many of these cases, particularly those ascribed to the liver.

Considering this evidence, there is no doubt in our minds as to the validity of the association found between cigarette smoking and cancer of the lung and the association found between smoking and cancer of other sites directly exposed to tobacco smoke products. The evidence also suggests that there is a real association between cigarette smoking and cancer of one or more sites in the genitourinary system. Considering the various sites within the genitourinary system, cancer of the bladder showed the highest degree of association with cigarette smoking.

The nature of the evidence is such as to leave doubt as to whether a real association exists between cigarette smoking and cancer of the gastrointestinal system (except esophagus). The apparent association could have arisen through misdiagnosis of primary site in some cases (e. g., primary cancer of the lung with metastasis to the liver being erroneously ascribed to primary cancer of the liver).

In seeking to evaluate the possibilities outlined above, one must keep three things in mind: (1) the likelihood of a physician mistaking one particular disease for another particular disease, (2) the number of deaths ascribed to each of the two diseases involved, and (3) the magnitude of the apparent association between smoking habits and each of the two diseases involved.

One example is sufficient to illustrate the point. Let us consider the hypothesis that the association found between cigarette smoking and death from coronary artery disease resulted from a confusion (in some cases) between coronary artery disease and lung cancer. A total of 5,297 deaths were ascribed to coronary artery disease, and there was a difference of 1,388 between the observed and expected number of deaths among men with a history of regular cigarette smoking. All told, there were only 448 deaths ascribed to lung cancer and most of these were microscopically proved cases. For the hypothesis to be correct, one must assume that at least 1,388 lung cancer deaths were missed as

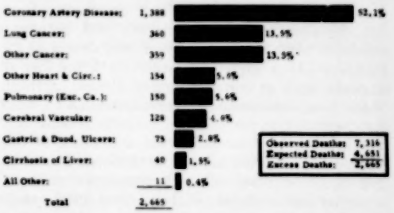

Fig. 9.—Excess deaths among men with a history of regular cigarette smoking.

such and were diagnosed instead as due to coronary artery disease. We leave it up to the reader to decide the likelihood of this occurring.

The most important finding of this study was the high degree of association between cigarette smoking and the total death rate (fig. 9). Errors in diagnosis, no matter how great, have no effect on this finding. Therefore, if the association found between cigarette smoking and deaths from some particular disease (e. g., cancer of the liver) was due to errors in diagnosis, it only means that the true degree of association between cigarette smoking and death from some other specific disease (e. g., lung cancer) is greater than the figures given in this report appear to indicate.

A total of 7,316 deaths occurred among men with a history of regular cigarette smoking, whereas only 4,651 would have occurred if the age-specific death rates of the smokers had been the same as for men who never smoked (fig. 9). The difference of 2,665 may be considered as "excess" deaths. Coronary disease accounted for 52.1% of the excess deaths among cigarette smokers; lung

cancer accounted for 13.5%; cancer of other sites accounted for 13.5%; other heart and circulatory diseases 5.8%; pulmonary diseases (other than lung cancer) 5.6%; cerebral vascular lesions 4.8%; gastric and duodenal ulcers 2.8%; cirrhosis of the liver 1.5%; and all other diseases combined 0.4%.

Summary

There is a high degree of association between total death rates and cigarette smoking, a far lower degree of association between total death rates and cigar smoking, and a small degree of association between total death rates and pipe smoking. The available source of information for this study, on diseases involved, was cause of death as recorded on death certificates, supplemented by more detailed medical information in cases in which cancer was mentioned.

The following relationships with cigarette smoking are evident: (1) an extremely high association for a few diseases, such as cancer of the lung, cancer of the larynx, cancer of the esophagus, and gastric ulcers; (2) a very high association for a few diseases, such as pneumonia and influenza, duodenal ulcer, aortic aneurysm, and cancer of the bladder; (3) a high association for a number of diseases, such as coronary artery disease, cirrhosis of the liver, and cancer of several sites; (4) a moderate association for cerebral vascular lesions; and (5) little or no association for a number of diseases, including chronic rheumatic fever, hypertensive heart disease, other hypertensive diseases, nephritis and nephrosis, diabetes, leukemia, cancer of the rectum, cancer of the colon, and cancer of the brain. The relative importance of the association listed above is dependent on the number of deaths attributed to each disease, as well as on their degrees of association with cigarette smoking.

It was found that the death rate of men with lung cancer who had given up cigarette smoking for a year or more before being enrolled in the study was lower than the death rate of men who were smoking cigarettes regularly at that time. An extremely high association between cigarette smoking and death rates for men with this disease was found in rural areas as well as in large cities. If smoking habits are taken into consideration, the lung cancer death rate was somewhat higher in cities than in rural areas.

521 W. 57th St. (19) (Dr. Hammond).

This study was made possible by the cooperation of the subjects, volunteer workers, state health departments, many physicians, and personnel of divisions of the American Cancer Society. Lawrence Garfinkel, M.A., Constance L. Percy, M.S., Leonard Craig, M.A., and Herbert Seidman, M.B.A., assisted in this study.

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DIABETIC NEUROPATHY.—Mimicry of diabetic neuropthy by coincidentally occurring pathology not specifically related to diabetes is not unusual. The reverse, namely, mimicry of many disease patterns by diabetic neuropathy, has frequently been recorded. How can this problem be resolved? At the present time, in view of the absence of any symptoms, signs, or laboratory findings pathognomonic of diabetic neuropathy, extreme caution must be exercised in diagnosis. The appearance of neurological abnormalities in a diabetic must perforce immediately suggest the diagnosis of diabetic neuropathy. Nevertheless, regardless of the frequency of this complication and the statistical probability of such diagnosis being correct, it should always be made with reservation. The diagnosis of diabetic neuropathy may be made only after the complete exclusion of any and all other possible explanations. If this be accomplished, then one may be more secure if the spinal fluid total protein is elevated and the course of the syndrome remains compatible with known experience. The definitive clarification of the diagnostic dilemma will not, in all probability, be reached via the strictly clinical approach. A more likely road to the goal of a pathognomonic feature may well lie in a further study of the spinal fluid abnormalities. It has long been recognized that in patients with diabetic neuropathy there is usually an elevation of the total protein content of the spinal fluid. The nature of this protein elevation, which protein fractions are involved, or whether there are abnormal proteins are problems currently under investigation. It is hoped that such studies will help clarify a confused situation.—Max Ellenberg, M.D., Diabetic Neuropathy: Pitfalls in Diagnosis, *A. M. A. Archives of Internal Medicine*, December, 1957.

MEDICAL ETHICS—CHOICE FOR RIGHT

Howard A. Nelson, M.D., Greenwood, Miss.

"A physician should be an upright man, instructed in the art of healing . . . modest, sober, patient, prompt to do his whole duty without anxiety; pious without going so far as superstition, conducting himself with propriety in his profession and in all the actions of his life."

Thus did Hippocrates write the first principles of medical ethics more than three centuries before the birth of Christ. In less than 50 words of classical Greek, he established the foundation for nearly all systems of ethics to follow, and in 22 centuries of writing and rewriting men have failed to add or take away a single tenet. The Hippocratic essentials are conduct, obligation, character, and aim.

Time has produced only an interweaving of moral declarations, science, and religion. Nothing really new has been added. This suggests something strangely wonderful about the profession of medicine: the manner in which it is practiced predates by thousands of years the science actually practiced. But there is then an important distinction to be made between morality and science. Ethical principles are a priori while science is empirical. But this for many scholars, even those who disagree among themselves, is a meaningful interdependence and not a cleavage. The apriorist calls for a distinction between reason and experience where the former consists of eternal principles of validity not derived from the latter. But experience must include morality. Two contemporary scholars of theology and ethics, Brightman,[1] an empiricist, and Knudson,[2] an apriorist, seem most representative of this view.

The young physician must be no less proficient in the humanities than he is in the sciences if he is to succeed in bringing his career into a rich perspective of character and competence. If he is deficient in either, he is not likely to become the doctor his preceptors are striving to make nor the one an enlightened public expects and demands. There is no documentation to back up this notion, but the chances are that no physician grounded in serious training in ethics, morality, philosophy, and religion will find himself before the medical society grievance committee or the board of censors.

Evolution in systems of medical ethics is virtually limited to manners of statement and application. For 21 centuries, they were individually stated and informally applied. During the past 100 years, medical ethics has become a collectively stated proposition formally applied by the body politic to the whole of the profession. Medicine came of age in the 19th century, and Percival's "Principles of Medical Ethics" in 1803 preceded the organization of the American Medical Association by only 44 years. Although the historic A. M. A. organizational meeting at Philadelphia in May, 1847, had the primary purpose of improving medical education, the founding fathers took time to adopt the first version of the familiar document.[3]

The present "Principles of Medical Ethics of the American Medical Association"[4] is not even twice as long as the oath of Hippocrates. It is a brief document of scarcely more than 500 words, a substantial reduction from the old 4,000-word Principles which existed in essentially the same form for 110 years. The chief difference in the versions is the elimination from the older document of the dicta of etiquette and manners formerly intermingled among guides for moral conduct and professional obligation. There is a word to be said for the old Principles which will be all but lost to the next medical generation. (The Judicial Council of the American Medical Association has published an "abstract of opinion" which reproduces all the sections of the 1955 edition of the Principles, correlating them to the 1957 edition.)

The young physician must be no less proficient in the humanities than he is in the sciences if he is to succeed in bringing his career into a rich perspective of character and competence. The doctor must also be a citizen, and must seek the ideal balance in community and professional living. The dignity and confidence enjoyed by the profession should be upheld, and methods of healing should be founded on a scientific basis. Evolution in systems of medical ethics is virtually limited to manners of statement and application. Most questions of ethics are answered simply by requiring that the physician's action be in the best interest of the patient, but the honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual but also to society.

President, Mississippi State Medical Association.

Read before senior students, University of Mississippi School of Medicine, Jackson, Miss., Sept. 23, 1957.

At some point early in his professional career, each young physician should read the older version. This is not a plea to reverse the June 6, 1957, action of the A. M. A. House of Delegates at New York and return to the old. It is an exhortation to the coming generation of physicians to grasp and hold to everything of possible value which the past can provide. Complex society has made uncertain the navigation channels in the turbulent sea of modern professional pursuits, and the lighthouses of moral guidance are altogether too far apart. No thinking medical leader is thus crusading for a return to the horse and buggy doctor so often lionized in the legend of ideals. This is, conversely, a rare opportunity to draw on the riches of the past, while avoiding its error, and to reap the profits of now-apparent mistakes.

Although remembered historically as a symbol of material splendor, Babylonia apparently gave the world the first formalized expression of medical ethics in the Code of Hammurabi, the benevolent despot who reigned from about 2123 to 2081 B. C. The celebrated code, engraved on a priceless and magnificent stele now in the Louvre at Paris, contains 282 sections providing for nearly every legal and moral problem of that ancient society. It even spelled out the physician-patient relationship! And that was as far from Hippocrates as his oath is from the 1957 version of the "Principles of Medical Ethics."

From Hammurabi to Hippocrates to New York is just about the history of the world, but the moral aim of the healer is consistent all along the way. The preamble to the "Principles of Medical Ethics" states, "These principles are intended to aid physicians individually and collectively in maintaining a high level of ethical conduct. They are not laws but standards by which a physician may determine the propriety of his conduct in his relationship with patients, with colleagues, with members of allied professions, and with the public."

That strength of character is a matter of self-determination obtains with the physician where it fails with others. The Principles are nothing more than a yardstick with which to measure conduct, obligation, and aim. Specifics are generally avoided, giving way to broad guiding principles. Except for eight words in section 5, there is no reference, direct or indirect, to professional freedom. Yet the whole of the document is a declaration of moral freedom—but only freedom to choose the right.

There is never a problem in ethics until the individual is confronted with a choice. Every choice we make commits us to consequences. At the precise instant the choice is made, we reach a point of no return. Some early moral codes provided generously for recalling poor choices through escape and exoneration devices following a determination of guilt.[3]

Roberts tells of a highly respected physician who was sure that lack of scientific medical knowledge had been disastrous to patients he was treating some years previously. The doctor had no fear of punishment and suffered no pangs of remorse because his treatment had been that which the medical profession of the day regarded as correct and acceptable. The doctor had no ethical or scientific alternative.[4] The important question arises, then; what is choice and what kind of situations compel us to make a choice? The answer is both eternal and temporal; morality is eternal, but the conditions of choice are temporal, based on empiricism of existing knowledge. For the ethical physician, there is never a point of turning back nor is there atonement. The choice he makes must stand as his best effort; to do less is to fail ethically.

The 10 sections of the current "Principles of Medical Ethics of the American Medical Association" deal with medicine's goals of service, improvements in knowledge and skills, and scientific attainment. Further, physicians are exhorted to uphold the dignity and confidence enjoyed by the profession and to safeguard themselves against incompetence within the profession. Responsibility to patients, disposition of services and professional attainment, and sources of income constitute principal ethical limitations. One section alone is given over to the physician-patient relationship, and a final injunction emphasizes the responsibility of the physician as a citizen and member of society. Sectarian or cultist relationships are strictly prohibited as being unethical.

The first section outlines medicine's aims: "the principal objective of the medical profession is to render service to humanity with full respect for the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion."

The words of Hippocrates ring in this simple and direct statement recalling that the physician should be "modest, sober, patient, prompt to do his whole duty without anxiety." It logically follows that in section 2 is demanded a continual striving to improve knowledge and skills, requiring that benefits of all professional attainments be made readily available to patients and colleagues alike. Thus does American medicine have a moral basis for prohibiting secret remedies and techniques; these are devices of the cultist, usually worthless, if not harmful. Not a few national-level organizations in medicine require certain postgraduate education minimums, thus insuring constant improve-

ment of scientific knowledge and skills. Meetings of the county medical society, state medical association, and A. M. A. are devoted principally to this necessary end.

In section 3 it is required that "a physician should practice a method of healing founded on a scientific basis; and he should not voluntarily associate professionally with anyone who violates this principle." This is the ethical basis for separation of cultism from science, superstition from knowledge. It is unethical to associate voluntarily in any manner with a chiropractor, naturopath, osteopath, or other irregular practitioner. Since 1955, when Resolution No. 77 was adopted by the A. M. A., the Judicial Council has held it unethical to associate voluntarily with an optometrist.[7]

One of the four cardinal hippocratic principles is specifically covered in section 4, which states, "The medical profession should safeguard the public and itself against physicians deficient in moral character or professional competence. Physicians should observe all laws, uphold the dignity and honor of the profession and accept its self-imposed disciplines. They should expose, without hesitation, illegal or unethical conduct of fellow members of the profession."

This injunction as to the physician's character raises the question of freedom of choice. More a matter of semantics than of morality, there is no question of being bound or free—only the question of by what the ethical physician shall be bound.[8]

Section 5 contains the only statement of freedom of choice permitting that "a physician may choose whom he will serve." Exception is made to provide for emergencies, and the ethical practitioner is enjoined against neglect of a patient once care has been undertaken. He may discontinue his services, apart from discharge by the patient, only after giving adequate notice. Solicitation of patients is forbidden.

Oddly enough, the sternest requirements of moral and legal responsibility are interwoven with the single statement of freedom. This is the one section of the Principles relating directly to most statutory provisions on patient neglect as well as that of patient solicitation through advertising or other public dissemination of self-laudatory information.

Generally, the basic unit of medical organization —the county medical society—exercises the greatest latitude in interpreting this section. Precisely what constitutes advertising, patient solicitation, and self-laudation is best determined at the local level. Appellate prerogatives are reserved to the state medical association and A. M. A. Judicial Council. The practice of local determination and definition of these unwholesome practices is not to say that the state association is without prerogative of original hearing and ruling; there are many instances where this has, indeed, been done.[9]

Corporate practice and exploitation of a physician through employment arrangements are primary subjects of interest in Section 6. It is stated, "A physician should not dispose of his service under terms or conditions which tend to interfere with or impair the free and complete exercise of his medical judgment and skill or tend to cause a deterioration of the quality of medical care."

This has been one of the most difficult portions of our system of ethics to interpret and enforce. Many physicians feel that the statement is vague and less than definitive. This lack of definition, however, permits state associations to examine problems in light of local conditions and permits them to elaborate upon that principle for the guidance of its membership. For example, the Mississippi State Medical Association works through its House of Delegates. This House of Delegates has made the following statement:[10]

> It is essentially undesirable for professional services to be purveyed by hospitals, corporations, and/or political subdivisions where fees for services are involved either from the patient or a responsible third party except for those statutorily established and medically accepted programs of government which are not disapproved by the association.
>
> Reasonably expeditious and conscientious effort should be exerted by all physicians to provide medical services privately, whether gratuitiously or paid, in a climate of free choice where possible.
>
> Patience and indulgence should characterize the efforts of all concerned to achieve these objectives without unnecessary delay. Litigation and the development of profound differences of viewpoint which, when publicly exposed, tend to lessen confidence of the people in the American system of medical care should be scrupulously avoided.

"In the practice of medicine," section 7 states, "a physician should limit the source of his professional income to medical services actually rendered by him, or under his supervision, to his patients. His fee should be commensurate with the services rendered and the patient's ability to pay. He should neither pay nor receive a commission for referral of patients. Drugs, remedies, or appliances may be dispensed or supplied by the physician provided it is in the best interest of the patient."

Here is the one reference to the economics of medical practice in this entire system of ethics. Previously, the older and longer version had a number of references, especially with respect to financial gain being a subordinate objective to that of service. It must be noted that there is no ethical taboo against the dispensing of drugs and appliances, but there is a strong qualification that such action must be in the best interest of the patient. Formerly, dis-

pensing was generally held as unethical; practical experience has demonstrated that this former restriction was not always in the interest of the patient.

Sections 8 and 9 require the exercise of moral judgment by the physician in the pursuit of scientific activity. The former requires that a physician seek consultation upon request, in doubtful or difficult cases, or whenever it appears that the quality of medical service may be thereby enhanced. Here is a situation where the physician must make a qualitative evaluation in ethical judgment.

Section 9 makes it incumbent upon a physician not to "reveal the confidences entrusted to him in the course of medical attendance, or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the individual or of the community."

Finally, in the "Principles of Medical Ethics" the physician is required to have a balance of conscience and a proper investment of emotional and civic capital. It states, "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community."

Perhaps the best commentary would be to say simply that the doctor must also be a citizen. It is good advice to the doctor for him to seek the ideal balance in community and professional living which avoids an exaggeration of moral consciousness just as it does that of incompetence. The heritage of medicine is rich, but the exacting requirements on the disciples of a sometimes inexact science make doctors servants of a "jealous mistress." [11]

To give your career to medical science, you must first give your life to morality and dedication.

308 Fulton St.

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GONADAL RADIATION DURING X-RAY THERAPY.—No matter what may be considered "safe doses" [of radiation], it is desirable to know how much radiation reaches the gonads of patients who receive routine dermatologic x-ray therapy with conventional equipment (and how this may be reduced or eliminated without reducing the efficacy of the therapy). Many variables and unexpected factors that increased or decreased the doses to the gonadal areas were discovered . . . and the dose to the gonadal area is not a predictable figure based on the roentgens delivered or the distance from the x-ray tube to the gonadal area, although these are important factors. . . . Efforts are being made to find the most effective means of eliminating, or at least reducing to a minimum, the amount of radiation reaching the gonads, without reducing the efficacy of the therapy. In this regard, factors under study include: 1) the most efficient types and methods of shielding, 2) the means for reducing secondary radiation from the table and other equipment beneath and about the irradiated area, 3) the positioning and tilt of the x-ray tube and methods of reducing the stray radiation from the tube head, 4) the effects of the position of the upright metal supports and the arm suspending the tube, and 5) the most effective placing of the patient to protect the gonads. . . . Further studies have demonstrated that, with care and relatively simple measures, it is generally possible to reduce by a substantial amount the radiation dose reaching the gonads during routine dermatological therapy.—V. H. Witten, M.D., M. B. Sulzberger, M.D., and W. D. Stewart, M.D., Studies on the Quantity of Radiation Reaching the Gonadal Areas During Dermatologic X-ray Therapy, *The Journal of Investigative Dermatology*, February, 1957.

DOCTORS AND POLITICS

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Although all doctors are individualists, they must take an active part in the political life of their communities and of the nation. In addition, physicians must emulate the tradition of the past if they wish to preserve the individual freedom which they expect as a natural consequence in their own practice. There is a direct parallelism between diseases of individuals and those of a community. People expect a doctor to take care of his civic responsibilities and they want and appreciate his advice.

In June, 1957, at the annual meeting of the American Medical Association in New York City, the House of Delegates adopted a revised "Principles of Medical Ethics."[1] Section 10 of those principles reads, "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community."

This is a statement on the positive side. It might be well to read into that section "and to prevent the deterioration of society to a socialistic level of governmentally controlled medical practice. Also, it should be the responsibility of the physician to oppose third-party intervention in all respects, no matter what their source."

Just a week later an article appeared in the Sunday edition of the Bridgeport (Conn.) *Herald* by Leo Gold[2] entitled "Is There a Doctor in the House?" in which the author went on to say that ever since someone stopped him and asked him "How come you rarely find a doctor taking part in city affairs and politics?" the question had bothered him. The article had to do with the situation in Stamford, Conn., where there are 155 doctors listed in the latest phone book and only 2 doctors in local politics—one on the zoning board of appeals and the other on the town housing authority.

The author felt that inadequate representation of doctors in city life has an indirect effect on the citizens of the town. While professional people such as lawyers and teachers devote much time and effort to the affairs of Stamford, the doctors are noticeable by their inactivity and seeming disinterest in the way things are going. He went on to say that of course some doctors are called out often late at night but that there must be others in the medical field who have a few spare moments to aid in the important job of ministering to city ailments. He doubted if doctors would say, "We don't have to do anything as far as city affairs are concerned. We have more important things to do."

Of the 40 members of the Board of Representatives in Stamford, not one is a doctor. Is it because its members had to run for office and had to tell of their qualifications in one form or another? To advertise, "Special—One Appendectomy—$100," is far different from stating one's qualification for an office. No physician is going to push his specialty in that manner. Gold ended his article by saying, "All this should not be construed too strongly as an attack against our healers. It is more a bid for physicians to step more actively in community affairs. The Stamford Medical Society might do well to encourage its members to become more identified with the community—and not to be solely satisfied with a doctor-patient relationship. The city needs all the help it can get and doctors should give a little more than just that which comes from the business end of a hypodermic." These are pretty strong words from a columnist, but unfortunately, they are true.

There are other sources much closer to home that have highlighted the fact that today doctors must play a larger role in community and national affairs. Dr. David Allman,[3] in his talk delivered at the Yale University School of Medicine during a course of lectures on "Economics in Medical Practice" given in January of last year, clearly brought out the fact that "the ivory tower of professional detachment is no longer tenable, or even possible, for the modern physician. His knowledge and his opinions are needed for the solution of too many problems which either affect his everyday activities, or may have a vital effect on the future of American medical practice. If the profession as a whole fails to take an active part in solving these problems, we shall be guilty of abdicating our full responsibilities as both physicians and citizens."

Further on in his article Dr. Allman states, "An alertness to the implications of legislation involving medicine is one of the profession's greatest needs at the present time. Whether we like it or not modern medicine has become involved in all the cross currents of public interest, public opinion and political action. In the 84th Congress, for example, 571 bills involving medicine were thrown into the hopper. With the increasing amount of

medical legislation in these times of social and economic change, medical organizations have a growing duty to study the issues, arrive at decisions and make their opinions known to both legislators and the public."

The doctor has a direct responsibility to his community. People expect a doctor to take care of his civic responsibilities and they want and appreciate his advice. You do not have to be an expert on community problems, but as a student of human psychology you can often arrive at the solution of a problem by the application of medical common sense. It is amazing to consider the parallelism between diseases of individuals and those of a community. Both individuals and communities are subject to attacks of hysteria for which the solution rests on firmness and strict adherence to the truth; both are subject to disorders of their drainage systems where occasionally there must be a primary resection or additional easier ways of relieving established back pressure; both are subject to attacks of aphasia; and both are subject to parasitic growths which may kill them. It would be interesting to carry this analogy further; some quite humorous parallels will suggest themselves to you.

There are surgical emergencies in the community which demand the same immediate drastic action usually associated with a ruptured viscus. There are the more slow types of community disease where procrastination and the trial-and-error method can be used. The experienced physician will quickly be able to determine the proper course of action in a community if he applies some of his medical knowledge to it.

Unfortunately, today, too many of the house staff and younger practicing physicians have become tongue-tied when it comes to talking or doing anything about politics. Some are afraid that they might antagonize patients and lose one or two; others are fearful that stating their ideas about anything outside medicine, baseball, or golf will brand them as "advertisers." Both of these ideas are wrong. Most people admire a man who states what he thinks or believes. They know where he stands, and generally it is felt that such a man will tell the truth about other things, such as whether a patient has cancer or needs an operation. As far as the "advertiser" idea is concerned it is usually a blind behind which the uninformed hide.

Doctors and Politics in the Past

It is extremely fortunate that physicians during the early days of this country had a different attitude about civic obligations and politics. Let us look at a few. Samuel Fuller [4] was a combination clergyman and doctor who came over on the Mayflower and practiced medicine in New England for 13 years, being for some time the only physician in that area. John Clark was expelled, with Roger Williams, from Massachusetts, and went with him to found the colony of Rhode Island, where in 1644 he became pastor of the first church as well as a practicing physician. Major political figures, including Thomas Wynne, a Welsh settler in Pennsylvania who became speaker of the First Provincial Assembly, and Thomas Lloyd, the first deputy governor of Pennsylvania, were also physicians. Three of the early presidents of Harvard were physicians: Charles Chauncy (1654), Leonard Hoar (1672), and John Rogers (1682).

A stormy figure in early Virginia was the surgeon John Pott, who arrived in 1621 and served as physician general and later deputy governor to the colony. Though himself a landowner, he stood with the small farmers against monopolization of the best tracts of land by the king's favorites. This attitude brought him up against Governor Harvey, a disagreeable type, who accused him of cattle-rustling and hog-killing and inciting the Indians, and assembled a jury that found him guilty. On Pott's appealing the verdict to England, Harvey had a second thought and intervened on Pott's behalf because he needed his medical skill, so that Pott was reinstated. A feud continued between them, however, for many years afterward.

One of the early "greats" of the New England medical scene was John Winthrop Jr.

Born in Groton Manor, England, in 1606 when his father was but eighteen years old, he developed into a magistrate, an industrial prospector, a scientist and a physician. He received the best instruction in Cambridge and Dublin, travelled extensively through Europe as part of his education, and in 1631 followed his father to this country where his record is one of glowing achievement. Characterized as eager, outgoing, genial, responsive, modern, John Winthrop, Jr., possessed the energy, optimism, and resourcefulness of the American pioneer. For eighteen successive years he was a magistrate of the Bay Colony, then, after a visit to England, he was engaged by Lord Say and Sele and by Lord Brook to establish a settlement near the mouth of the Connecticut River. With his eagerness for industrial possibilities he was attracted to Pequot (now New London). Eight years after the death of his father, he was elected Governor of Connecticut and moved to Hartford. The scientific tastes and attainments of this most popular gentleman are evidenced by the fact that he possessed a library of over one thousand volumes, for a century the best scientific library in the English colonies.[5]

These men were imbued with the idea of personal freedom. They were educated men, trained in the classics, generally well travelled, and distinctly individualistic in their ideas and actions. Today, it seems that we are abandoning the principles and practices of personal freedom. Instead of fearing and limiting the power of government, we act as if centralized power, compulsion, and over-all planning were the source of our economy. Power is granted to the government upon any request and then we seek favors while at the same time increasing our tax burden to the point of bankruptcy. If you should ask yourself, "Do you

want the power of the federal government to increase further and spend more of your money without your representation?" you would undeniably answer, "No." "The mainspring of human progress is individual liberty, and individual liberty decreases as federal power increases."[6]

The latest and most interesting article published on doctors and politics is the report of Dr. Thomas Alphin.[7] He brings out the fact that there is nothing improper or new in physicians' taking an active part in our government. Indeed, when the electorate calls, it is a sacred duty on a par with medicine's highest precepts to help in the good health of your fellow men.

You may not realize it, but there were five physicians who signed the Declaration of Independence. The second signer was Dr. Josiah Bartlett of New Hampshire, an able and ardent patriot. Previously, he had been ousted from his post as justice of the peace by the royal governor of New Hampshire and had seen his home burned to the ground. In 1776, as delegate to the Continental Congress from New Hampshire, he was the second person to sign the engrossed document at the formal ceremony on Aug. 2. The other four were Drs. Lyman Hall (for Connecticut), Benjamin Rush, Matthew Thornton, and Oliver Wolcott. These five doctors were to achieve a degree of immortality as symbols of the strong interest of the medical profession in the preservation of individual freedom.

This is not the whole story of the doctor in national politics. Since the signing of the Declaration of Independence, there have been 359 physicians who, over the years, have helped to shape the destiny of the country as members of the United States House of Representatives and Senate. The story is interesting and in some ways revealing. For example, at least 13 also were state or territorial governors, and three states selected men from this group as their first governors.

It is a tribute to the medical profession that in every congress since 1775 there has been at least one physician as a member. At present, there are six physicians who are members of the 85th Congress. The large states that were members of the original 13 colonies naturally have supplied the most doctors to Congress. Leading the list is Pennsylvania with 52. Next are New York with 48 and New Jersey with 30. Ohio, although coming into the union later, has sent 26 doctors to Congress. Other totals are Georgia, 17; Kentucky, 12; Maryland, 16; Massachusetts, 13; Missouri, 10; New Hampshire, 14; Virginia, 18; and North Carolina, 11. Connecticut has elected six, Delaware seven, Illinois five, Indiana seven, Louisiana five, Michigan five, South Carolina five, and Tennessee eight. It seems from looking over this scoreboard that the Far West has not yet awakened to the possibility of sending doctors to Congress.

Conclusion

The gist of these observations is this: It is high time that doctors take an active part in the political life of their communities and of the nation and emulate the tradition of the past if they wish to preserve the individual freedom which they expect as a natural consequence in their own practice. All doctors are individualists, but it would seem that today the synoptic attitude of doctors of the past has been transformed into a myopic lethargy and that eventually they will not be able to see further than the cocoon that has been spun about them during their resting period.

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DISSEMINATION OF THE SPIRIT OF SCIENCE.—Human life is now permeated with science; human civilization rests upon scientific foundations. Yet the vast majority of our people have little understanding of science as a way of thinking or a method of seeking answers to problems. Superstitious awe of the magician—yes, there is far too much of that—but of the avowed adoption of a scientific approach to all sorts of human problems, woefully little. Politically it has been demonstrated that a house divided against itself cannot stand. I affirm that it must also be true that a nation of a microscopically few scientists molding and altering the lives of people, and a populace uncomprehending, superstitious, and resisting likewise cannot endure. Somehow, and soon, mankind must become truly scientific in spirit and in endeavor.—H. B. Glass, The Responsibilities of Biologists, *The American Institute of Biological Sciences*, November, 1957.

ARTERIAL GRAFTING IN SEVERELY ISCHEMIC LEGS

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About 30% of patients who were admitted for possible amputation of their leg were found to be suitable for arterial grafting procedures. Arterial grafts may obviate the necessity for amputation in a significant percentage of patients with gangrenous or pregangrenous lesions of their extremities. Attempts at grafting in many patients of the type described in this paper will inevitably result in some failures. Amputation should not ordinarily be undertaken for arterial occlusion unless arteriograms have demonstrated the fact that the patient would not be helped by a grafting procedure or where, clinically, the obstruction is so far distal as to make arteriograms unnecessary because the vessels are too small to graft.

The problem presented by patients having ischemic legs and either pregangrenous or frankly gangrenous changes in the feet is familiar to all physicians. Since the introduction of arterial grafts, the outlook for these patients has become more favorable. Early experience [1] indicates that, with arterial grafts, amputation may be avoided in a significant proportion of such individuals. Although some authors [2] feel that arterial grafting procedures generally should not be attempted when gangrene exists, our experience and that of others [3] indicates that it is proper to attempt such procedures when possible.

At the hospital of the University of Pennsylvania during the years 1955 and 1956, one of us (B. R.) has either personally operated on or assisted members of the resident staff in operating on 20 patients in whom arterial grafts were used and who had either gangrene of a portion of the foot or pregangrenous changes. Under pregangrenous changes we have included two conditions, (*a*) ischemic ulcers which have shown no evidence of healing under a rigid program of "medical" therapy and (*b*) ischemic "rest pain" of sufficient severity to warrant amputation.

Of the 20 patients, 8 had gangrene of one or more toes, and 12 had either rest pain or ischemic ulcers. Three of these 12 patients had acute arterial occlusions that were not embolic in nature. Of the 20 patients, 15 would have had prompt amputation if the graft had not been attempted. The remaining five could have had conservative therapy continued on their ischemic ulcers, at least temporarily, had they not been subjected to grafting. During this same two-year period 34 patients who were judged to be unsuitable for grafting on the basis of arterial studies had amputations. Thus, grafting procedures were attempted in 15 of 49 patients, or 30% of those patients presenting themselves with conditions justifying prompt amputation of the leg.

In table 1 the pertinent information about the 20 patients has been summarized. One patient (case 7) had two operations performed three months apart because of acute occlusions that developed in his femoral artery. The second occlusion did not develop in the graft but in a previously patent portion of his femoral artery. A new graft was sutured end to end with the old one, and both remained patent a year later. Thus, there were 21 grafting procedures done, and 19 of them were immediately successful. Nine patients with immediately successful procedures have developed further arterial occlusions subsequent to operation, one of these being the patient in case 7. Of the remaining eight patients, three have since come to amputation. Of the remaining five who have avoided amputation of the leg, none have died. Of the 15 patients who were faced with immediate amputation, 10 are still using their leg, and 3 had temporary relief ranging from one week to three months before further occlusion occurred and amputation became necessary. Of the two with immediate graft failure, both had subsequent amputation, and one has since died. There was one operative death. This occurred in an 82-year-old woman (case 17) who died two weeks postoperatively of multiple arterial emboli of unknown origin.

Four of the 20 patients suffered from known diabetes at the time of operation. Grafts were successfully used in all of these patients, but two have since developed further occlusion, one at 3 months and one at 10 months after operation. Of the 21 grafts used, 4 involved the aorta, 1 was of the iliac artery, in 15 the proximal end was anastomosed to the femoral artery, and 1 involved the popliteal artery alone.

In three patients preoperative x-ray examination of the distal arterial tree was not made. In the remaining 17, satisfactory arteriograms were obtained preoperatively. In only two patients was the so-

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called run-off of the distal vessel considered good. The other 15 patients were classified as either fair or poor in this regard.

These patients were elderly and had long standing progressive ischemic changes, except for one patient (case 4), a 13-year-old boy whose case

Fig. 1.—*Left*, preoperative condition of foot of patient in case 8. *Right*, condition of same foot, seven months postoperatively.

summary is given below. Excluding this patient, the average age of the group was 66 years and the mean age 65. If the boy is included in the series, the average age is still 63.

Report of Cases

The following four cases are given to illustrate the types of problems encountered.

Case 8.—An 86-year-old man was admitted to the hospital of the University of Pennsylvania on Dec. 22, 1955, for amputation of his left leg. This elderly diabetic patient had had severe pain in his foot for approximately nine months. Six weeks prior to this admission he had been treated in the hospital without significant improvement of his foot, and after discharge he developed progressive gangrene in his first toe. On examination there was no pulse in the left leg below the femoral, but the right popliteal pulse was palpable. The left foot was cool and exhibited the findings shown in figure 1, *left*. On admission the patient was receiving 45 units of isophane insulin daily. A femoral arteriogram showed extensive changes in the femoral artery and a complete block approximately 5 cm. long involving the lower portion of the femoral and the upper portion of the popliteal artery. The popliteal artery, though patent, appeared to have a poor run-off. In spite of this fact, however, an arterial graft was attempted. A 9-cm. freeze-dried arterial homograft was inserted by use of the by-pass technique.

The patient withstood the procedure well, and his foot promptly became warm, although no pulses were palpable in it. Five days later weak pulses were first palpated in both the dorsalis pedis and posterior tibial arteries. By this time the toes had improved considerably in appearance. Two months later the fifth toe had healed, and the great toe had improved further. Nine months postoperatively the great toe had nearly completely healed, and the pulses remained. One month later, the patient had developed further occlusion, and the lesion on his great toe had deteriorated. The distal end of the toe has remained open since that time, but the ulceration has not extended, and this man is still able to walk and use his foot.

In retrospect we believe that prompt amputation of the gangrenous portion of the patient's great toe should have been carried out after the successful grafting procedure. Had this been done and the toe allowed to heal completely while the circulation was relatively good, it is likely that it would have remained healed following later deterioration of his circulation.

Case 19.—A 73-year-old man was admitted to the hospital on July 30, 1956, because of gangrene of three toes of his right foot. After an injury to his second toe in February, 1956, he developed gangrene in this toe, and he was admitted to another hospital where it was amputated. The amputation site did not heal but became infected, and three of the four remaining toes became gangrenous. Figure 2, *left*, shows the appearance of his foot at the time of his admission to the university hospital. At this time he was in severe pain. No pulse was palpable below the femoral artery on either side. The rest of his physical examination was within normal limits for a man of his age. He was not diabetic. His arteriogram revealed a 9-cm. block in the right femoral artery with a patent popliteal artery and a fair run-off. A 20-cm. freeze-dried arterial homograft was therefore inserted as a by-pass graft extending from the femoral artery to the popliteal. Postoperatively his foot became warm, and it was thought that transmetatarsal amputation might be successfully accomplished. This was done five days after the arterial graft. On the following day the posterior tibial pulse was first palpated. The flaps left by the transmetatarsal amputation were closed secondarily, and the wound healed nicely.

Two and one-half months after the arterial graft had been done, the patient was readmitted because of the recurrence of pain in his foot. A portion of the skin at the amputation

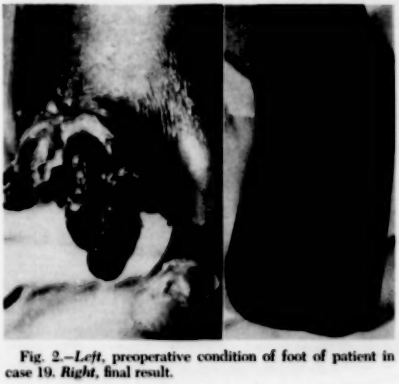

Fig. 2.—*Left*, preoperative condition of foot of patient in case 19. *Right*, final result.

site had opened, and his foot was again cool. No pulse was palpable below the femoral artery, and a new arteriogram demonstrated that the graft had become occluded. A lumbar sympathectomy was then done, and the open area gradually healed. The foot has since remained healed. Figure 2, *right*, shows the appearance of the foot six months postoperatively.

TABLE 1.—*Summary of Pertinent Information on Twenty Patients Undergoing Arterial Grafting*

			Preoperative State					Type of Surgery		Clinical Results				
Case No.	Sex	Age, Yr.	Findings	Candidate for Immediate Amputation	Diabetes, Yr.	Other Evidence of Severe Vascular Involvement	Run-off Shown by Arteriogram	Type of Graft	Site	Immediate Result	Late Failure	Further Surgery	Present Condition	Length of Follow-Up, mo.
1	M	52	Acute occlusion; impending demarcation of four toes; rest pain	Yes	...	None	...	Arterial homograft	Left aortic-iliac; right aortic-iliac; sympathectomy	Success	Thrombosis, 18 mo. (one iliac)	None	Slightly better than preoperative before acute occlusion	28
2	M	56	Ischemic ulcer; rest pain	Yes	...	None	Fair	Arterial homograft; venous autograft	Left aortic-iliac; right aortic-femoral; sympathectomy	Success	...	None	Foot healed; intermittent claudication (1¼ blocks)	28
3	M	75	Gangrene in second toe	Yes	...	Myocardial infarction	Poor	Arterial homograft	Left femoral-popliteal	Failure; supracondylar, 3 days	...	None	Stump healed	25
4	M	13	Acute occlusion; impending gangrene of anterior tibial muscles	Yes	...	None	...	Arterial homograft	Left popliteal-popliteal	Success	...	Muscle slough	Leg healed	15
5	M	66	Ischemic ulcer; rest pain	Yes	...	None	Poor	Arterial homograft	Left femoral-popliteal; sympathectomy	Success	Thrombosis, 11 mo.	Amputation of fifth toe, ¼ month	Varicose ulcer healing slowly	15
6	M	68	Gangrene in first, fourth, and fifth toes; rest pain	Yes	...	None	Fair	Arterial homograft	Left external iliac; sympathectomy	Success	...	Amputation of fourth toe, 2 mo.	Foot healed	14
7	M	72	Acute occlusion; impending gangrene; rest pain; anesthesia; paralysis	Yes	...	Hypertension; congestive failure	...	Arterial homograft	Left middle femoral; lower femoral	Success	Thrombosis, own vessel, 3 mo.	Further grafting, 3 mo.	...	14
7	M	72	Similar to above, but another area involved	Yes	...	Hypertension; congestive failure	...	Arterial homograft	Left high femoral; middle femoral	Success	...	None	Comfort at rest; pedal pulse	11
8	M	86	Gangrene in first and third toes	Yes	1	None	Fair	Arterial homograft	Left femoral-popliteal	Success	Thrombosis, 10 mo.	None	Ischemic ulcer of first toe	14
9	F	64	Gangrene in third toe; ischemic ulcer	Yes	6	None	Poor	Arterial homograft	Right femoral-popliteal	Success	...	Amputation of fourth toe, ¼ month	Ulcer healed	13
10	F	70	Intermittent claudication (⅛ block); ischemic ulcer	No	¼	None	Good	Arterial homograft	Left aortic-popliteal; right aortic-femoral; sympathectomy	Success	...	None	Ulcer healed	13
11	M	73	Gangrene in fourth toe; demarcation all toes	Yes	...	Arteriosclerotic heart disease	Poor	Venous autograft	Right femoral-popliteal	Failure; supracondylar amputation, 1 mo.	...	None	...	Death, 2 mo.
12	M	63	Ischemic ulcer	No	...	None	Poor	Arterial homograft	Right femoral-popliteal	Success	...	None	Ulcer healed	10
13	M	73	Ischemic ulcer; rest pain	No	...	Myocardial infarction	Poor	Arterial homograft	Right femoral-popliteal	Success	...	None	Ulcer healed	10
14	M	65	Ischemic ulcer	No	...	None	Fair	Arterial homograft	Left femoral-popliteal	Success	Thrombosis, 7 mo.	Sympathectomy, 9 mo.; supracondylar amputation, 10 mo.	Stump healing well	10
15	M	55	Gangrene in heel, rest pain	Yes	...	Cerebral and cardiac arteriosclerosis	Good	Arterial homograft	Left aortic-iliac; right aortic-iliac; sympathectomy	Success	...	None	Ulcer healed	9
16	F	82	Demarcation of all toes; rest pain; anesthesia	Yes	...	Cerebral and cardiac arteriosclerosis	Poor	Venous autograft	Right femoral-popliteal	Success	...	None	...	Death, ½ mo.
17	M	59	Ischemic ulcer; rest pain	Yes	13	Myocardial infarctions	Poor	Arterial homograft	Left femoral-popliteal	Success	Thrombosis, 3 mo.	Supracondylar amputation, 3 mo.	Stump healed	6
18	M	55	Ischemic ulcer; rest pain	No	...	Cerebral and cardiac arteriosclerosis	Fair	Arterial homograft	Left femoral-popliteal	Success	Thrombosis, ½ mo.	None	As before	6
19	M	73	Gangrene in four toes	Yes	...	None	Fair	Arterial homograft	Right femoral-popliteal	Success	Thrombosis, 3 mo.	Transmetatarsal amputation, ½ mo.; sympathectomy, 5 mo.	Walking; comfortable	6
20	M	56	Gangrene in one toe	Yes	...	Myocardial infarction	Poor	Arterial homograft	Right femoral-popliteal	Success	Thrombosis, ¼ mo.	Supracondylar amputation, ½ mo.		4

This case illustrates clearly the advisability of prompt excision of gangrenous tissue following grafting in order to give the wound a chance to heal while the circulation is improved. We doubt that sympathectomy alone would have permitted the transmetatarsal amputation to heal had it been done as the primary procedure when the foot was grossly infected.

CASE 4.—A 13-year-old boy was admitted to the hospital of the University of Pennsylvania on Nov. 10, 1955, because of impaired circulation in his left leg. He had been in his usual state of good health until three days before, when during a football game he sustained an anterior displacement of the distal left femoral epiphysis. Two unsuccessful attempts at reduction had been made elsewhere prior to his admission to this hospital, at which time he had a temperature of 101 F (38.3 C) and a pulse rate of 100. The unusual physical findings were confined to his left leg. No pulse was palpable below the femoral artery, and the leg was edematous, pale, and cold below the knee. Motion and sensory perception of the ankle and foot had been lost. The hemoglobin level and leukocyte count were normal.

The patient was taken to the operating room promptly after admission, and the disrupted left popliteal space was explored. A simple separation of the distal femoral epiphysis and a complete severance of the popliteal artery were found. The popliteal vein, surprisingly, was still intact. The peroneal nerve was severely contused. After the damaged portion of the popliteal artery had been excised, a 6-cm. freeze-dried arterial homograft was inserted end-to-end, and, following removal of the soft tissue caught between the bone ends, the epiphyseal separation was readily reduced and held with sutures. At the time of the closure of the incision, the arterial flow through the graft appeared satisfactory, and its pulse was good. A long plaster splint was applied to the leg.

On the first postoperative day, the foot remained cool and became more edematous. By that evening a severe erythematous reaction developed over the anterior tibial muscles. A fasciotomy was therefore performed and nonviable portions of the muscle groups were excised. After this procedure, the foot became warmer and developed a good color. On the 3rd postoperative day a posterior tibial pulse was first palpated, and on the 10th postoperative day a dorsalis pedis pulse could be felt, in spite of the fact that the anterior tibial artery had been destroyed and removed along with the anterior tibial group of muscles. During the next five weeks all remaining portions of the anterior tibial group of muscles sloughed out along with most of the interosseous membrane. In spite of antibiotics the patient continued to have fever for five weeks and then began to drain necrotic material from the popliteal wound. It was then apparent that his calf muscles had also become necrotic. Therefore the calf muscles were exposed and removed. After this procedure the patient gradually became afebrile, and his wounds slowly healed.

When the patient was examined 15 months after injury, his pedal pulses were still present. He had full use of his knee but no voluntary motion of his ankle, which is partially fixed by fibrosis in the position of function. The skin and bone appeared normal, but the patient had lost essentially all striated muscle in his lower leg. He wears a brace to prevent foot-drop and even runs very well on this leg. In fact, he recently was able to pitch a no-hit-no-run baseball game.

This boy was the only patient in the series having an occlusion for reasons other than spontaneous thrombosis. His is a problem that is very different from the rest and resembled more the type of situation seen in battle casualties. The prolonged period of ischemia apparently produced irreversible damage in his muscles, but changes in the bone were reversible. It was of great interest to us that he did not have thrombosis throughout the distal arterial tree after 72 hours, but this fact is probably related to the healthy state of his vessels prior to injury.

CASE 10.—A 70-year-old woman, complaining of intermittent claudication in both legs, was admitted to the university hospital on Jan. 12, 1956. It had begun seven years before and now was produced by walking one-half of a city block. In addition, she had a persistent ischemic ulcer on her left heel. The significant findings on physical examination were limited to her legs. No pulses were palpable below the waist, and the skin of both feet was atrophic.

The ischemic ulcer of the left heel was approximately 1.5 cm. in diameter and had been present for many months. Laboratory studies and neurological examination were normal. An aortogram revealed occlusion of the right common iliac artery near the aortic bifurcation and separate occlusions of both the left internal and external iliac arteries. Femoral arteriograms done by operative exposure of the profunda femoris vessel showed the left femoral artery to be completely occluded, but the popliteal artery appeared to be relatively normal. The right femoral artery was occluded in its middle third. One week after admission the patient was operated on, and an aortic bifurcation homograft was inserted as a by-pass. By suturing graft to graft, extensions were carried down to the left popliteal and to the right superficial femoral arteries where they were anastomosed to these vessels. This patient made an uneventful recovery and has maintained the patency of her graft. The ulcer on her left foot healed promptly, and she has been greatly relieved of claudication.

We were willing to operate upon this patient because there appeared to be an excellent run-off in her lower leg. It is seldom that one finds such a situation in patients having ischemic ulcers of the foot unless the arterial block is high, as in this case. This patient was not threatened with immediate amputation but had had progressive difficulty and was anxious to avoid further progression of her ischemia.

Comment

Attempts at grafting in many patients of the type described in this paper will inevitably result in some failures. As a group, these patients are not favorable for grafting, and generally their arteriograms make this fact abundantly clear. When the alternative is amputation, however, few of us would not willingly undergo such an operation as arterial grafting if there was significant hope of success and thereby avoidance of amputation. Humphries and others [1b] stated that they were able to save one leg in five, under these circumstances, and felt that even 20% success was sufficient to warrant operating. More recently [1c] they are saving the legs of approximately one of every two such patients.

Other reports [4] have shown varying degrees of success, but there is little question that amputation can be avoided in some patients. The circulation seldom can be restored to normal in such patients,

but it may be improved to such a degree that normal function is restored and prompt healing of wounds takes place. Because of this fact we believe that amputation should not ordinarily be undertaken for arterial occlusion unless arteriograms have demonstrated the fact that the patient would not be helped by a grafting procedure or where, clinically, the obstruction is so far distal as to make arteriograms unnecessary because the vessels are too small to graft.

As time goes on, additional patients will doubtless develop late occlusions, but this fact does not mean that the grafting procedures were not worthwhile. In patients of this type, a "delaying action" against the progress of their vascular disease and the restoration of function for even a relatively short time may be very worthwhile, and the longer the period of restoration of function the better. Even if the graft becomes occluded, the benefit of the grafting procedure may continue when the use of the graft permits the healing of an open ulcer or an area previously involved with gangrene. Some of these wounds remain healed if and when the circulation is again reduced. Two of our patients demonstrated this type of response. Less circulation is required to maintain a foot with its skin intact than one in which there is an open ulcer. It is for this reason that the healing of an ulcer of the foot may be the deciding factor as to whether or not amputation will be ultimately required, and it is for this reason that it is important to do promptly any minor amputation that may be required after a graft has been successfully inserted. One never knows how long it may be before other occlusions may occur, and therefore any steps necessary to insure reasonably prompt healing of wounds that may be present in the extremity should be taken. In addition, even in patients in whom amputation may subsequently become necessary following a temporarily successful grafting procedure, there is a more ready acceptance by the patients of amputation since they feel that everything possible has been done to avoid it.

In the selection of patients for arterial grafting, the display of an adequate run-off by the arteriogram is of unquestioned importance. This factor has been emphasized by many authors,[5] but, because of the desperate state of some of these patients, one is justified in operating upon them under circumstances that would not be felt suitable for elective procedures. Many of the patients in this series, as shown in table 1, had arteriograms demonstrating poor run-off, and we have been repeatedly surprised that their grafts were even initially successful. Although an optimistic prognosis is not fully justified when we discuss the problem with these patients, the majority of patients request that we attempt to restore flow, even when they are aware of the high incidence of early or late failures that is seen in these situations.

In the hope of preventing early thrombosis of these grafts or of the patients' vessels, heparin sodium was used in the immediate postoperative period, except in cases where the abdominal cavity had been opened. In two of these patients hematomas in the thigh developed postoperatively, but in neither case did it interfere with the function of the graft. As a group, these patients with advanced ischemia would appear to be more likely to develop thrombosis than the average patient subjected to grafting. If satisfactory long-term anticoagulant therapy were more readily achieved, it would be useful in these patients. The benefit, or lack of benefit, attendant on prolonged anticoagulation is very difficult to assess accurately, but the rationale for its use is similar to that for long-term anticoagulant therapy for coronary occlusions.

The location of the arterial block is of some importance in assessing the likelihood of success in any grafting procedure. The cumulative experience[6] indicates that the larger the vessel that is grafted the more likely it is to remain patent. The results of grafts in the aorta and the common iliac arteries generally are better than those in the femoral or popliteal vessels. No statistically significant conclusion can be drawn from a series as small as the one presented here, but the same trends are indicated. Likewise, the more intrinsically healthy the vessels are the more likely they are to remain open. Except for the boy (case 4), the only patients in the series that had nearly normal distal vessels were two of the patients having aortic obstructions.

The relationship of diabetes to arterial disease has long been appreciated, and it has likewise been known that arterial changes associated with diabetes are apt to be widespread. This diffuse vascular involvement of diabetes renders many of these patients unsuitable for vascular grafting. Fewer patients among diabetics have been found to be suitable candidates for grafting than among an equal number of nondiabetics. Nevertheless, the decision for or against grafting in an individual patient is not significantly influenced by the presence or absence of diabetes. This decision should be made on the basis of the condition of the patient generally, the condition of the leg, and the condition of the vasculature as shown by the arteriogram.

Much has been written[7] in recent years about the best type of arterial graft. Clinically we have used only autogenous vein grafts or arterial homografts. In our hands the arterial homograft has been more satisfactory in the type of patient presented here. Without evidence from a well-controlled study, it has been our impression, based on both our experience and that reported by others,[8]

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that there is a higher incidence of immediate failure if one uses venous autografts rather than arterial homografts (table 2). The higher incidence of early failures may be related to two factors, namely, local spasm of the vein wall which results in the reduction of the lumen and consequent diminution of flow through the vessel and also the liberation by the living graft of thromboplastin or similar substances that lead to thrombosis following injury of living tissue.

This tendency for vein grafts to occlude is shown in table 2, which indicates the comparative results of arterial and venous grafts as compiled from some recent reports. If, however, a peripheral artery is grafted successfully with an autogenous vein, the graft is probably less likely to develop late difficulties than is any other type of graft. Some long-term follow-up studies [9] of venous autografts of peripheral arteries have shown these grafts to be capable of acquiring the histological appearance of an artery and of functioning as an artery for many years without trouble when they are supported by surrounding muscle.

TABLE 2.—*Recent Reports on Failure of Venous and Arterial Grafts*

	Vein			Artery		
	Total	Failure, No.	Failure, %	Total	Failure, No.	Failure, %
Shaw and Wheelock [7b]	13	8	61	13	2	15
Hoye and Warren [8a]	13	8	61	16	12	75
Linton [6a]	22	10	45	68	13	19
DeTakats [7a]	...	...	30	...	...	10
Szilagyi and Overhulse [3]	...	...	...	...	...	20 immediate 20 late
Crawford and others [1a]	...	...	...	101	9	9
Horton [2]	...	...	...	28	18	64
Easteott [11]	...	...	...	13	7	54
Humphries and others [1b]	...	...	...	120	30	25
Dye and others [5]	30	19	63	...	...	...
Lord and Stone [9]	9	5	56	...	...	...

The technical aspects of grafting are also of importance in determining success or failure of the procedure. The use of the by-pass graft as advocated by Linton,[6a] Crawford and co-workers,[1a] and Laufman and co-workers [10] has some advantages over the end-to-end suture method which makes it desirable to use in most cases. By being able to use any area of a vessel that seems most suitable for suturing, one often avoids the dilemma of having either to suture the vessel in an area that may not be good or to destroy some collateral circulation. A considerable extent of a vessel in areas that are known to be patent has often been exposed before finding a suitable site for anastomosis. By using a by-pass graft one can avoid destruction of collateral vessels lying between the block and the anastomotic site.

Such a method also permits a large anastomosis to be made in small vessels, but it does lack the theoretical advantage of direct flow with less turbulence as obtained with an end-to-end suture. An end-to-end suture at one end of the graft and an end-to-end suture at the other may be used if such seems advantageous. We strongly believe, however, that clamps should not be used on arteriosclerotic vessels that are smaller than the aorta, for thrombosis may result from their use even in the common iliac arteries. Tapes may be placed around the vessels and tightened just enough to occlude the flow of blood. They are far less traumatic than the most gentle clamps and less apt to cause damage.

Sympathectomy was not used often in these patients, but when used in conjunction with a grafting procedure it has, on occasion, seemed to add more than we would normally have anticipated. During intra-abdominal procedures, it is relatively simple to remove the sympathetic chain. However, if a femoral or popliteal graft is used, the addition of a lumbar sympathectomy increases the magnitude of the procedure considerably, and usually a sympathectomy was not done in addition to the graft. However, to do this more often might extend the period before a late occlusion takes place and also add a further increment to the arterial flow. The possible advantage that might be derived from the addition of sympathectomy should not be overlooked when using vascular grafts.

Summary

Arterial grafts may obviate the necessity for amputation in a significant percentage of patients with gangrenous or pregangrenous lesions of their extremities. Approximately 30% of patients who were admitted for possible amputation of their leg were found to be suitable for grafting procedures. A series of 20 such patients had 21 operations, two of which were immediate failures. Three of the 19 patients with successful grafts have subsequently developed further thrombosis requiring amputation of their leg.

Any gangrenous tissue should be excised promptly if a graft is successfully inserted in order to reestablish an intact skin barrier as soon as possible. Further arterial occlusions after a successful operation are common but may not necessitate amputation of the limb if the skin is then intact. Diabetes is not of itself a contraindication to this type of surgery. The possible further advantages of sympathectomy used in conjunction with grafting should not be overlooked.

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CLINICAL NOTES

SUPPRESSION OF GROWTH IN EXCESSIVELY TALL GIRLS

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Until recently, there has been little or no documentation in medical literature of therapeutic attempts to check the excessive height of growing girls. In 1956, Goldziehr [1] reported a definite inhibition of skeletal growth by prepuberal estrogen administration in a series of 14 girls.

Excessive height in girls is not nearly as embarrassing as it was a number of years ago, inasmuch as tall girls have achieved some prestige in the entertainment world, in modeling, and in beauty contests. Nevertheless, some tall young girls are self-conscious about their height because of the great difference between them and their classmates and friends. These girls will often slump or stoop in an attempt to appear less conspicuous. This report is concerned with two such girls whose skeletal growth was inhibited by use of estrogens. By bringing this procedure to the attention of physicians, it is hoped that girls whose height is embarrassing to them may receive medical aid in preventing continued rapid growth.

Report of Cases

CASE 1.—A girl, aged 12, had a height of 64.5 in. (163 cm.). She had been growing at the rate of about 2.5 in. (6 cm.) per year. Since she had not yet attained puberty, it could be predicted that she would eventually grow an additional 3-4 in. (7-10 cm.) or more. Her bone age at this time was normal, and there were no other evidences of a glandular dysfunction. A dose of 4.5 mg. of conjugated estrogenic substance was administered daily by mouth. There was an almost immediate suppression of growth, since by the end of six months she had grown only 0.5 in. (1 cm.). At this time, she reported a continuous light uterine bleeding. It was not determined whether this was related to true menstruation or to the possible hyperplasia endometrii due to the estrogen administration. It was explained to the mother that this bleeding might continue for some time, that it would not harm the child, and that, were the estrogens withdrawn to stop the bleeding, her normal rapid growth would probably resume. Therefore, estrogen therapy was continued. The patient bled irregularly for the next five months, after which a cyclic flow took place every 29-32 days. One and one-half years after the commencement of treatment, her height was 66.25 in. (168 cm.). At this time, her skeletal bone age was equal to that of a 16-year-old girl. She grew only 0.12 in. (0.32 cm.) in the next six months, and, since her bone age was that of a nongrowing girl, treatment was stopped. At the end of another six months, her height had not increased, and the patient was discharged with a total growth of about 1.75 in. (4 cm.) in two years, compared to a predicted increment of 3 to 4 in. (7 to 10 cm.). Regular menstrual periods continued subsequently.

CASE 2.—A girl, aged 11½, had a height of 66.38 in. (169 cm.) and was approximately 5 in. (12 cm.) taller than most of her classmates. She was growing at the rate of 3 in. (7 cm.) per year. She was seen prepuberally, and her bone age was normal. It was estimated that she would probably grow at least an additional 4 in. (10 cm.). Conjugated estrogenic substance in doses of 2.5 to 3.75 mg. was administered daily by mouth. At the end of six months, her height had increased 0.5 in. (1 cm.), showing a definite suppression when compared with her previous rate of growth. At the

end of another six months, she had grown an additional 0.63 in. (1.5 cm.), reaching a height of 67.5 in. (171 cm.). Six months later, her height was 68.12 in. (173 cm.), and five months later her height was still this amount. Her bone age at this time was equal to that of a 15 or 16-year-old girl. In view of the apparent leveling off of her growth, therapy was stopped. However, eight months later, she had grown an additional 0.5 in. (1 cm.). This was unexpected in view of her bone age, but it did demonstrate the suppressing effect of the estrogens. However, 68.63 in. (174 cm.) was her final height, since she has not grown in the year prior to writing. Thus, her total increase in height was 2.25 in. (6 cm.), compared to the predicted minimum of 4 in. (10 cm.). Seven months after the onset of administration of estrogen, she developed uterine bleeding which persisted for about three months. After this bleeding had stopped, she commenced menstruating regularly and has continued to do so ever since. There was no breast pain in either girl.

Comment

It is considered that these two patients had a successful growth inhibition. It is, of course, impossible to state what their final growth would have been had not estrogen therapy been instituted. However, in view of the previous rate of growth and its immediate suppression after onset of treatment, one is justified in claiming that they would have been considerably taller had they not received this therapy.

The mechanism of growth suppression by estrogen has probably two physiological bases. It has been shown experimentally, for instance, that estrogens suppress growth hormone elaboration in the pituitary of rats. The second mechanism by which estrogen therapy suppresses growth is probably in action on the growth centers in the bones themselves. Thus, x-ray evidence in both of the above reported cases showed that after one and one-half to two years of treatment with estrogen the bone age was advanced four to five years in both cases. A similar condition is observed in precocious puberty, where an actual stunting of growth occurs through bone aging induced by endogenous estrogens. Goldberg and I [2] demonstrated that after suppression of endogenous estrogens by androgen administration in one patient stunting was eliminated and the girl achieved a height of 63 in. (160 cm.) compared to an average of approximately 56 in. (142 cm.) in untreated patients.

The results herein reported on estrogen administration for suppression of growth duplicate closely those reported by Goldziehr.[1] In view of the satisfactory response to this therapeutic procedure and the absence of serious side-effects, this seems to be an effective and safe method of checking rapid growth in excessively tall girls.

Summary

Two girls were treated with estrogen to inhibit their growth. In both cases, the eventual height was considerably less than what might be predicted were the patients to have remained untreated. There were no harmful effects in either patient other than some irregular uterine bleeding. Regular menstruation occurred following cessation of therapy.

450 Sutter St.

References

1. Goldziehr, M. A.: Treatment of Excessive Growth in Adolescent Female, J. Clin. Endocrinol. 16:249-252 (Feb.) 1956.

2. Freed, S. C., and Goldberg, M. B.: Constitutional Precocious Puberty in Female and Its Control by Androgens: Preliminary Report, J. Clin. Endocrinol. 8:1081-1087 (Dec.) 1948.

MENTAL RETARDATION.—It is unlikely that in this country there is any other form of disability which equals impairment of mental ability in respect to its toll of economic uselessness and human misery. If one uses as the criterion of disability the inability to obtain gainful employment, one can say that, with the possible exception of mental illness, mental retardation is the most significant handicap of our present society. To be specific, of the 4,200,000 children born annually in the United States, 3% (126,000) will never achieve the intellect of a 12-year-old child, 0.3% (12,600) will remain below the 7-year intellectual level, and 0.1% (4200), if they survive, will spend their lives as completely helpless imbeciles, unable even to care for their own creature needs. . . . This is a problem which we have always had with us, but a number of factors have served recently to reemphasize its importance. The first of these is the increasing complexity of our society and the development of programs of compulsory education. Both of these have served to alter the definition of retardation and to cause to be included within this category persons who would not previously have been considered handicapped. An additional factor is the increase in our ability to deal with other forms of illness. As our adequacy in treating the acute infectious diseases of childhood has increased, our inadequacy in treating the disorders of the nervous system stands out in sad contrast.—R. L. Masland, M.D., The Prevention of Mental Retardation, *A. M. A. Journal of Diseases of Children*, January, 1958.

THE WINDSHIELD INJURY

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One of the injuries peculiar to automobile accidents is the windshield injury—multiple, irregular lacerations of the face sustained when the victim strikes the windshield. These injuries are notoriously deceiving. All too often, wound margins are carefully sutured and primary healing is achieved, yet in a few weeks the initial smooth, fine scars have widened or become hypertrophic and the margins are inverted, rolled, elevated, or otherwise distorted. A pleasing repair at the operating table becomes a source of disappointment to the physician and distress to the patient. Secondary repair becomes necessary.

While it is true that unsatisfactory scars can be improved by later surgical revision, it is equally true but more significant that satisfactory results can be achieved from primary repair if the causes of the subsequent problems are understood and eliminated at the time. The purpose of this paper is to point out the pitfalls in the repair of windshield injuries and offer suggestions for improved results.

Before progressing directly to the problem, it should be emphasized that in any injury the total picture must be kept in mind. When life is endangered by the magnitude of the injury, definitive repair of facial injuries can and should be temporarily delayed until the general condition of the patient is stabilized.[1] Arrest of hemorrhage, restoration of blood volume, and establishment of an adequate airway are basic. Anesthesia must be adequate, either general or generous local. Finally, repair of underlying bone and nerve injury must precede soft tissue repair.[2] However, the scope of this paper will be limited to problems of skin closure.

Principles of Wound Closure

One often hears that a poor wound closure has "caused a scar" or that subsequent surgery can "get rid of a scar." Such statements are, of course, erroneous. Scar tissue is the normal and essential end-product of repair. It is not the mere presence of scar tissue that determines the result of repair but the quality and quantity of the scar, as well as the direction and degree of subsequent scar contracture. Surgical repair, therefore, should be done with the aim of minimizing scar formation and adjacent skin distortion.

The basic principles of closure of face wounds, regardless of etiology, are the same as for wounds elsewhere on the body. All wounds must first be thoroughly cleansed and, where necessary, débridement should be done. Débridement is a well-accepted principle intended to convert a contaminated wound into a surgically clean one.[3] This procedure must be meticulous, with care being taken to avoid injury to the branches of the facial nerve. Ragged margins are excised; crushed tissue is removed. In addition to being fertile ground for infection, crushed tissue gives rise to fibrous tissue, contributing to scar hypertrophy. While débridement on the face must be conservative, it is false economy to save crushed tissue, as it will probably have to be removed at a later date. After débridement, hemostasis must be secured, dead space eliminated, and the wound closed.

For wound closure, suture material must be fine: 0000 plain absorbable surgical suture for buried sutures, 00000 or finer silk or nylon sutures for the skin. Landmarks, such as eyebrow or lip margins, are united first. Subcutaneous sutures should approximate skin edges as completely as possible so that there is minimal tension on skin sutures. Small absorbable surgical sutures placed just below the dermis are helpful for this. Skin sutures are not intended to draw the wound together; they are used to achieve the final accurate approximation of the skin margins. They should be placed close to the margins and close together. A good rule of thumb is ⅛ in. from the margins and ⅛ in. apart. A continuous subcuticular stitch may be used if desired. If the subcutaneous tissues have been closed well, the skin sutures can be removed early, starting on the third day, to avoid or minimize suture marks. Too large "bites" with too large suture material tied too tightly and left in too long produces the unsightly suture marks often associated with scars. A collodion dressing is useful after suture removal to support and immobilize the wound.

Types of Laceration

But why, as stated previously, are the scars from windshield injuries often so disappointing, even when accepted standard procedures have been followed? The answer involves some of the characteristics of these injuries and the fact that scars contract in the direction of the wound. This is best explained by examining some of the commonly encountered problems.

Oblique Laceration.—One of the characteristics of windshield injuries is the direction of the lacerations in relation to the skin surface. Although

some cuts may be perfectly perpendicular, more commonly they are oblique. The oblique lacerations may produce one of the major pitfalls in repair of injury. At the time of repair the skin margins lie flat, but, since scars always contract in the direction of the wound, one side eventually elevates or "rolls," as illustrated in figure 1*A*. Although the resulting ridge may be only a millimeter or two wide, the deformity is quite noticeable on an otherwise smooth skin surface. This ridge will flatten a little in time, but rarely will the margins flatten completely. The most meticulously performed closure cannot insure against this physiological process. The only effective measure is to create perpendicular skin margins by actual excision, as shown in figure 1*B*. Any subsequent contracture will then affect each margin equally.

Trap-Door Laceration.—Another common wound is V-shaped or U-shaped—the "trap-door" laceration. Scar contracture in these injuries causes elevation of the central segment of skin, as illustrated in figure 2*A*. Where possible, this wound is best handled by elliptical excision of the central segment, as shown in figure 2*B*. It is particularly important to carry this out when, as is often the case, the margins of the wound are severely oblique. When the central segment is too large to excise, the margins are made perpendicular by excision and the wound is closed.

Avulsion.—Occasionally in a segment of skin and subcutaneous tissue partial or total avulsion occurs. When avulsion is only partial, every effort must be made to save the segment if any circulation is evident. Because the face has an excellent blood supply, tissue in which partial avulsion has

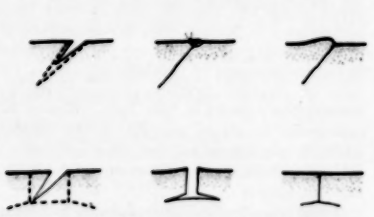


Fig. 1.—Repair of oblique laceration. *A*, scar elevates on one side due to contraction in direction of wound. *B*, effective closure creates perpendicular skin margins by actual excision, so that contracture affects each margin equally.

occurred has a remarkable ability to survive, even when the attachment is quite narrow. If some circulation is present, the flap, after necessary débridement, should be returned to its bed and a pressure dressing applied to reduce venous congestion. When the segment is obviously nonviable, or when complete avulsion is present, wound closure must be effected by other means. Under no circumstances should the wound be left open if the patient's general condition will permit surgery. Because of the elasticity of facial tissues, closure can frequently be accomplished by undermining the adjacent skin and advancing the margins.

Fig. 2.—Repair of "trap-door" laceration. *A*, contracture causes elevation of central segment of skin. *B*, effective closure is done with use of elliptical excision of the central segment.

When the defect is too large for this, a skin graft will prevent scar contracture and distortion of facial features. Any necessary revision can be carried out at a later time.

Multiple Small Lacerations.—A shattered windshield often inflicts a multitude of small lacerations which elevate tiny tags and flaps of skin. These often leave a disfiguring nodular irregularity of the skin surface. Treatment at the time of injury is limited. The larger tags can be excised and handled as "trap-door" or oblique lacerations. When lacerations are too small or numerous for this, the problem may have to be treated later when the nodularity can be improved by dermabrasion.

Abrasions.—In addition to the sharp lacerations due to the windshield injury, there often are associated abrasions. Not infrequently, gravel, grease, or other foreign material has been ground into the wound. If this is not completely removed, a disfiguring tattoo will remain. Generous saline solution irrigation is useful; a grease solvent is sometimes necessary. A scrub brush is very rough; a surgical sponge is preferable. A no. 11 Bard-Parker scalpel is useful for loosening foreign material. Although sometimes tedious, thorough débridement of these wounds is essential and rewarding.

Summary

Windshield injuries present many pitfalls to successful repair. A poor result affects the patient's morale and his social and economic outlook. Satisfactory results can be achieved from primary repair, however, reducing or eliminating the need for subsequent scar revision. The key to most problems is adequate débridement, creating perpen-

dicular wound margins. Avulsions are closed by returning viable flaps, undermining and approximating remaining tissues, or applying skin grafts. The problems of abrasions and multiple small lacerations are resolved by use of the same principles.

110 E. Main St. (3).

Illustrations were provided by Leslie G. Kilpatrick, M.D.

References

1. Masters, F.; Georgiade, N.; Horton, C.; and Pickrell, K.: Treatment of Soft Tissue Trauma of Face, J. A. M. A. 156:105-109 (Sept. 11) 1954.
2. Backus, L. H.: Treatment of Facial Lacerations, Indust. Med. 24:207-208 (May) 1955.
3. Young, F.: Care of Soft Tissue Injuries, New York J. Med. 43:1521-1526 (Aug. 15) 1943.

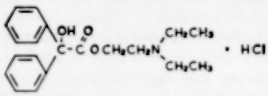
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Benactyzine Hydrochloride.—2-Diethylaminoethyl benzilate hydrochloride.—The structural formula of benactyzine hydrochloride may be represented as follows:



Actions and Uses.—Benactyzine hydrochloride, a diphenylmethane, is an anticholinergic compound with the same actions and effects but with approximately only one-fifth to one-fourth the activity of atropine. Benactyzine, however, usually produces an effect on the central nervous system with doses that elicit little or no peripheral effects. The mechanism of central action is not known, although observations in experimental animals tend to support the assumption that the drug acts on the hypothalamus in such a manner as to raise the threshold of emotional reaction to external stimuli. In rats subjected to mental stress, benactyzine increases the number of conditioned responses to a fixed stimulus. In normal human test subjects, therapeutic doses produce prompt subjective effects variously expressed as retardation of mental activity, blocking of thought, and feeling of muscular relaxation. Dizziness and ataxia may also occur. Objectively, the electroencephalogram shows a reduction in normal rhythm and sometimes abolition of alpha waves. This abolition coincides with the height of subjective effects. Because the drug does not exhibit sedative or hypnotic action and does not affect body temperature or blood pressure, it is not considered a tranquilizing agent in the sense in which that term applies to drugs that exert a depressant action.

Benactyzine hydrochloride is proposed for clinical use as a psychotherapeutic agent in the management of psychoneurotic disorders with anxiety reaction, obsessive-compulsive reaction, or mild depressive reactions. In general, it is stated that optimal benefits are more likely to occur in patients whose attitude is cooperative, whereas patients with a hostile attitude may deteriorate under therapy. Also, short-term neuroses which may have remissions tend to respond better than chronic, fixed disorders. It must be borne in mind that, as with certain other agents, psychoneurotic manifestations in some patients will occasionally be enhanced after use of benactyzine. Reports of clinical investigations are somewhat contradictory regarding effectiveness of the drug in the conditions for which it is proposed. Some observers feel that it is less effective than other psychotherapeutic drugs but may be more effective than the barbiturates in dealing with psychoneurotic symptoms. The drug appears to have practically no effect in the management of psychotic symptoms. On the basis of currently available evidence, the use of benactyzine appears to have been followed by improvement in about one-half of the patients in whom it was employed, but more conclusive clinical observations are necessary to establish its ultimate usefulness.

Benactyzine hydrochloride appears to have a low toxicity in both animals and man. In human subjects, experimental doses of 60 mg. daily for one month, or 90 mg. as a single dose, did not reveal serious toxic effects. The effect of the drug appears promptly after administration, and perceptible effects produced by a single oral dose of 5 mg. disappear within one to one and one-half hour. The drug is eliminated rapidly, chiefly in the urine. The

brain appears to retain the drug longer than other tissues, but there is no apparent residual action or accumulation.

Because of its anticholinergic nature, benactyzine hydrochloride may give rise to side-effects similar to those of atropine. Side-effects so far reported include dryness of the mouth, metallic taste, blurred vision, inhibition of accommodation, dizziness, giddiness, ataxia, nervousness, palpitation, nausea, diarrhea, general apathy, and indifference. When present, such effects may disappear with slight reduction in dosage. The chief subjective complaints are usually diminished ability to concentrate and a sense of depersonalization or unreality. In some patients, these may be sufficiently disturbing to warrant cessation of therapy to avoid intensifying the neurotic state. Other patients may complain of excessive muscular relaxation, with heaviness and paresthesia of the limbs. Prior explanation of such effects may reduce the unfavorable response in some patients.

Benactyzine hydrochloride is contraindicated in patients who are frankly hostile. The drug is also considered to be contraindicated in glaucoma because of its anticholinergic properties. Benactyzine hydrochloride should not be administered to patients who are to receive electroshock therapy. As with all new drugs, physicians should be alert to the possibility of untoward effects, which may appear with more extensive use.

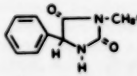
Dosage.—Benactyzine hydrochloride is administered orally. The suggested initial oral dosage for adults is 1 mg. three times daily for two or three days. If such doses elicit no therapeutic response, they may be increased gradually to 3 mg. three times daily. Administration after meals is considered desirable to minimize the occurrence of side-effects arising from unusually prompt absorption. Should side-effects occur at a particular dosage, it should be reduced. Dosages totaling more than 10 mg. daily are not considered desirable for any patient. However, until longer experience has been gained, the dosage of the drug should be considered tentative, and all patients observed carefully for the development of untoward effects.

Preparations: tablets 1 mg.

Applicable commercial name: Suavitil.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of benactyzine hydrochloride.

Ethotoin.—3-Ethyl-5-phenylhydantoin.—The structural formula of ethotoin may be represented as follows:



Actions and Uses.—Ethotoin, a hydantoin-type anticonvulsant, is useful for the treatment of grand mal epilepsy. The therapeutic dosage of ethotoin is greater than that of many commonly used anticonvulsants, such as diphenylhydantoin, primidone, or phenobarbital. On the other hand, ethotoin is considerably less toxic than any of the foregoing drugs and, unlike the barbiturates, does not produce sedation at therapeutic dosage levels. When used alone in grand mal epilepsy, it generally brings about a reduction in seizure frequency but may not always afford complete seizure control. It may be useful as a substance to try first, particularly if immediate control of grand mal seizures is not essential for social or economic reasons. If full control of the seizures is not obtained by use of ethotoin alone, it may be combined with other anticonvulsant drugs. In certain patients, it will control seizures that are refractory to other anticonvulsant agents. Ethotoin is of limited usefulness in psychomotor seizures. It has been tried in cases of petit mal and petit mal variant seizures. Although its usefulness is limited in this type of epilepsy, it may bring about improvement in some cases.

Ethotoin appears to have fewer side-effects than the other hydantoin derivatives in common use as anticonvulsants. In clinical trials over long periods of time and with high dosage, no evidence of kidney, liver, or hematopoietic damage has been observed. Only rare instances of ataxia or gum hyperplasia have occurred, and these reactions were found in patients undergoing treatment with other hydantoin derivatives. Occasionally encountered side-effects include skin rash, dizziness, anorexia, nausea and vomiting, diplopia, drowsiness, numbness, headache, tension, epigastric burning, nystagmus, gastrointestinal upset, and depression. Many of these side-effects respond promptly to a reduction in dosage; gastric distress may be minimized if the drug is administered with food. Although ethotoin appears to be a substance of low toxicity, the possibility of serious untoward reactions should be kept in mind, pending the accumulation of more clinical experience.

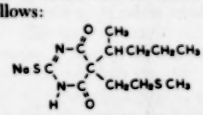
Dosage.—Ethotoin is administered orally in dosages which must be individualized according to the response of the particular patient and the degree of control achieved with other anticonvulsant drugs. The average dose for adults is 2 to 3 Gm. per day, given after food, in four to six divided doses. Dosages below 2 Gm. a day have proved ineffective in most adult patients. It is generally advisable to avoid a high initial dose. The recommended procedure is to begin treatment with not more than 1 Gm. daily and to increase the dose gradually over a period of several days, in order to determine the patient's individual tolerance and the optimal dosage. Doses as high as 5 Gm. a day have been used but are seldom necessary. When doses this size are required, it is considered wise to supervise the patient more closely.

Doses of 0.5 to 1 Gm. daily have been found effective in many children. However, amounts of 2 Gm., or more rarely 3 Gm., have been used successfully. An appropriate dosage will depend to some extent on the age and weight of the child and on the type and dose of concomitant medication. As with adults, it is considered advisable to start with a comparatively low dosage which may be increased gradually.

If the patient is already receiving another anticonvulsant medicament, it should be continued when ethotoin is started. Usually the dosage can be gradually reduced as that of ethotoin is increased, until ethotoin has replaced the previous medicament or until the optimal dosage of both anticonvulsants has been established. When ethotoin is combined with other hydantoins, the dose of the latter should be gradually reduced in order to avoid ataxia and other side-effects which occur with high doses of such other hydantoins.

Preparations: tablets 250 mg. and 500 mg.
Applicable commercial name: Peganone.
Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of ethotoin.

Methitural Sodium. — 5-(1-Methylbutyl)-5-[2-(methylthio)ethyl]-2-thiobarbiturate. — The structural formula of methitural sodium may be represented as follows:



Actions and Uses.—Methitural sodium, an ultra short-acting thiobarbiturate, is used as an intravenously administered anesthetic agent. Since its potency is less than that of thiopental sodium, larger doses are required to produce the same degree of anesthesia. Like other thiobarbiturates, methitural is stored temporarily in body fat depots and subsequently is transported to the liver, where it is metabolized. Because its metabolic degradation and excretion proceed more rapidly than those of thiopental, cumulative effects are less and awakening time is more rapid. These differences are more apparent when larger amounts of the drug are used for longer operative procedures. Anesthetic induction time is longer with methitural and should proceed more slowly than with thiopental.

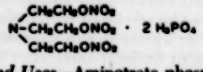
Methitural sodium is employed for the same purposes as the sodium salts of thiopental, hexobarbital, and thiamylal. Thus, it may be used as the sole anesthetic agent in short operative procedures, for induction prior to the administration of gaseous general anesthetics in long operations, and as a supplement to local anesthetics during regional and spinal anesthesia. The drug does not provide muscle relaxation but is compatible with and may be used in conjunction with curare and curariform drugs. Belladonna alkaloids should be administered as premedication. Once sufficient experience has been gained in the use of methitural sodium, general anesthesia with this agent appears to be as smooth and as satisfactory as that obtained with thiopental. Its diminished cumulative effects and rapid awakening time are considered advantageous. There is also some indication that methitural produces somewhat less postanesthetic "hang-over" than the other thiobarbiturates. On the other hand, parasympathomimetic effects, such as hiccups, coughing, and laryngospasm, seem to be greater with methitural than with thiopental. These effects plus increased induction time and venous irritation with concentrated solutions constitute disadvantages.

Side-effects to methitural sodium are those of intravenously administered barbiturates in general and include hypotension, respiratory depression, hypoxia, laryngospasm, and excitement. The drug should be used with caution in patients with dyspnea, asthma, respiratory obstruction, severe hypotension or hypertension, myocardial disease, cardiac decompensation, anemia, and extreme obesity. It is contraindicated in patients with severe hepatic dysfunction. Methitural should be administered only by anesthesiologists competent in the use of thiobarbiturates in intravenous anesthesia; equipment and facilities for providing oxygen and insuring adequate respiration should be available at all times.

Dosage.—Methitural sodium is administered intravenously. Except for concentration and dosage, the techniques and procedures for the intravenous administration of methitural sodium are the same as for other thiobarbiturates. For intermittent administration, the most satisfactory concentration appears to be a 2.5% solution; 5% solutions have been used, but at this concentration venous irritation is likely to be encountered. For induction of general anesthesia in adults, 4 or 5 cc. of a 2.5% solution is injected at intervals of 30 to 60 seconds. Although the rate of injection and dosage vary, the administration of 200 to 600 mg. in this manner is usually sufficient to induce anesthesia in most patients. After induction, small maintenance doses (2 or 3 cc. of a 2.5% solution) may be injected at intervals governed by the usual signs relating to depth of thiobarbiturate anesthesia. The total dosage of methitural should probably not exceed 2 Gm. in most patients. The drug may also be administered by slow intravenous drip of a 0.5 to 0.8% solution to supplement other forms of anesthesia.

Preparations: powder (injection) 1, 2, and 5 Gm.
Applicable commercial name: Neraval Sodium.
Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of methitural sodium.

Aminotrate Phosphate.—Triethanolamine trinitrate diphosphate.—The structural formula of aminotrate phosphate may be represented as follows:



Actions and Uses.—Aminotrate phosphate, an organic nitrate compound, produces a mild but persistent vasodilating effect on smooth muscle, especially that of the smaller blood vessels of the postarteriolar vascular bed. As with other agents in this category, this effect is believed to be dependent on the release of nitrite ion in the body. The drug also produces some degree of coronary vasodilation as indicated by its ability to improve blood supply and to relieve myocardial ischemia in the isolated rabbit heart. In human patients, clinically demonstrable effects referable to coronary vasodilation are not apparent until some time after administration of the drug. Thus, aminotrate phosphate is considered to be much slower acting than either glyceryl trinitrate (nitroglycerin) or amyl nitrite. On the other hand, its coronary vasodilating effects are much more prolonged than those produced by either of these agents. In contrast to most organic nitrates, aminotrate phosphate does not, in therapeutic doses, appreciably lower blood pressure or cause reflex tachycardia.

Aminotrate phosphate has been used prophylactically in the hope of preventing attacks of angina pectoris in patients subject to this disorder. Although few of the clinical reports available to date are well controlled, it is the impression of most observers that the drug is beneficial in reducing the frequency and severity of anginal attacks in some patients. However, therapeutic response to the drug appears to be variable and unpredictable; whereas some patients experience decided improvement under therapy, many others obtain no relief whatsoever. Although it is not possible to determine the precise percentage of patients in whom a favorable response might be expected, currently available evidence suggests that this will not exceed 50% and may be considerably less. Aminotrate phosphate shows about the same order of effectiveness as pentaerythritol tetranitrate. Because of its slow onset of action, aminotrate phosphate is not suitable for the immediate relief of anginal pain and is not intended to replace glyceryl trinitrate for this purpose.

Aminotrate phosphate appears to be better tolerated than most of the other nitrates used in the therapy of angina pectoris. Thus, the headaches, dizziness, gastric upset, nausea and vomiting, and palpitation which frequently complicate therapy with the other agents are encountered only infrequently. Although methemoglobinemia is a rare complication of nitrate therapy, aminotrate phosphate is believed to be safer in this respect for patients with anemia. Aminotrate phosphate increases intraocular pressure and is contraindicated in the presence of glaucoma.

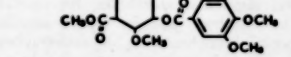
Dosage.—Aminotrate phosphate is administered orally. Although development of tolerance has not been reported, such an effect is to be expected on the basis of previous experience with other long-acting nitrates and physicians should be on the alert for it. Present evidence suggests that the dosage for aminotrate phosphate can remain constant for considerable periods without loss of effect. For the prophylaxis of angina pectoris, the usual daily dose is 8 to 16 mg. taken in divided doses before meals and before retiring. Somewhat larger doses have occasionally been employed. There may be no significant effect before the third day of administration, and a period of a week or more may elapse before maximal effects are apparent.

Preparations: tablets 2 mg. and 10 mg.; tablets (sustained-release) 10 mg.

Applicable commercial names: Metamine, Nitretamin.

Thos. Leeming & Co., Inc. and E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of aminotrate phosphate.

Deserpidine.—11-Desmethoxyreserpine.—The structural formula of deserpidine may be represented as follows:



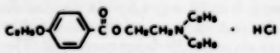
Actions and Uses.—Deserpidine, an ester alkaloid isolated from Rauwolfia canescens Linn., is identical in chemical structure to reserpine except that it lacks the methoxy (CH_3-O-) group at the 11 position. The pharmacological actions of deserpidine are essentially the same as those of other active alkaloids of Rauwolfia, including reserpine. On the basis of animal experiments and some clinical observations, deserpidine is said to have a more rapid onset of action than reserpine, is somewhat less potent, and produces less lethargy and depression. However, these minor differences are probably of little clinical significance from the standpoint of over-all effectiveness or dosage requirements, and both drugs have the same uses and limitations. (See the monograph on reserpine in New and Nonofficial Drugs.)

Dosage.—Deserpidine is administered orally. For the treatment of mild anxiety states and mental disturbances, doses of 0.1 mg. per day may be sufficient. At least 2 to 3 mg. daily is required for the treatment of institutionalized patients with psychosis. For the treatment of mild essential hypertension, the initial dose is 0.25 mg. three or four

times daily until the desired response has been obtained. Thereafter, blood pressure may be maintained with doses of as little as 0.25 mg. per day.

Preparations: tablets 0.1, 0.25, and 1 mg.
Applicable commercial name: Harmonyl.
Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of deserpidine.

Parethoxycaine Hydrochloride.—2-Diethylaminoethyl *p*-ethoxybenzoate hydrochloride.—The structural formula of parethoxycaine hydrochloride may be represented as follows:



Actions and Uses.—Parethoxycaine hydrochloride is a local anesthetic agent with actions similar to those of procaine. Its acute toxicity in experimental animals is slightly more than that of procaine. Parethoxycaine is rapid-acting, and the duration of anesthesia is slightly longer than that produced with an equal amount of procaine. In animal experiments, the drug appears to be somewhat more potent, milligram for milligram, than procaine. Except for these minor quantitative differences, parethoxycaine hydrochloride behaves pharmacologically in essentially the same manner as procaine hydrochloride.

Parethoxycaine hydrochloride is proposed for use in regional anesthesia by either infiltration or nerve block techniques, including dental procedures, for single injection or continuous spinal anesthesia, for peridural segmental anesthesia, for caudal anesthesia in obstetrics, and for topical anesthesia in cystoscopic, bronchoscopic, or endotracheal procedures. Clinical experience with the drug for all of the foregoing procedures has been too meager to permit definite conclusions as to its efficacy and safety. On the basis of limited studies conducted almost two decades ago, the drug appears to be about as satisfactory as procaine for those techniques involving parenteral injection, but it does not possess any advantages which would distinguish it from procaine, lidocaine, tetracaine, or any of the other local anesthetic agents that have undergone much more extensive clinical investigation.

When the drug is employed by the low spinal route, the onset of sensory anesthesia appears to be somewhat more rapid than with procaine. However, the duration of such anesthesia is not proportional to dose. Thus, in spite of its slightly increased potency, dosage of parethoxycaine for long operative procedures approaches that of procaine. The drug should not be used as a spinal anesthetic for operations above the lower abdomen. There is no clinical evidence to support its use for topical or surface anesthesia of mucous or other membranes.

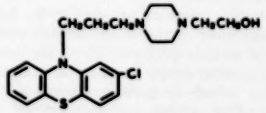
On the basis of limited clinical experience, parethoxycaine appears to be of about the same order of toxicity as procaine. The drug does not produce irritation at the site of injection but does elicit the same type of effect on blood pressure, pulse, and respiration which is observed after administration of procaine and similar local anesthetic agents. It should therefore be employed with the same discretion as all other agents in this category. (See the general statement on local anesthetics in New and Nonofficial Drugs.)

Dosage.—For regional anesthesia, the concentration of parethoxycaine hydrochloride solution and the amount injected vary according to clinical indications and the duration and extent of anesthesia desired. A 0.3 to 1% solution is proposed for infiltration anesthesia, whereas a 1 to 1.5% solution is suggested for nerve block techniques. For dental procedures, by either infiltration or nerve block techniques, a 1% solution has been used. Epinephrine hydrochloride, in a final dilution of 1:200,000, may be added when desired to solutions of parethoxycaine hydrochloride used in regional anesthesia. For single injection spinal anesthesia, a 2.5% solution may be employed; dosage varies from 0.6 to 2 cc. (15 to 50 mg.). A 2.5% solution of the drug in cerebrospinal fluid is employed for continuous spinal anesthesia; the suggested initial dose is 4 to 6 cc. (100 to 150 mg.) followed by 1 to 2 cc. (25 to 50 mg.) as needed. For peridural segmental anesthesia, 2.5 cc. (50 mg.) of a 2% solution is administered. Concentrations of 1.5% are suggested for caudal anesthesia. The proposed dosage for topical anesthesia of mucous membranes, as in cystoscopic, bronchoscopic, and endotracheal procedures, is 5 cc. of a 2 to 5% solution. Since there is no evidence to confirm the usefulness of parethoxycaine as a topical anesthetic, the foregoing proposed dosage for this purpose should be considered experimental.

Solutions of parethoxycaine hydrochloride become cloudy when exposed to air; hence, suitable dilutions of the sterile crystalline drug should be freshly prepared and used at once.

Preparations: crystals (injection) 1 Gm.; ointment 2% and 5%; solution (injection) 20 mg. in 1 cc., 50 mg. in 1 cc.
Applicable commercial name: Intracaine Hydrochloride.
E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of parethoxycaine hydrochloride.

Perphenazine.—2-Chloro-10-{3-[4-(β-hydroxyethyl)piperazinyl]propyl}phenothiazine.—The structural formula of perphenazine may be represented as follows:



Actions and Uses.—Perphenazine, a phenothiazine compound, differs chemically from prochlorperazine only with respect to the substitution of a

hydroxyethyl group for the methyl group of the latter drug. Perphenazine is approximately twice as potent, milligram for milligram, as prochlorperazine and exhibits depressant actions, clinical uses, and side-effects similar to those of chlorpromazine. Thus, perphenazine is useful in the treatment of psychoneuroses predominantly characterized by anxiety, tension, and agitation, in certain psychotic disorders, for the control of hiccough, and also as an antiemetic for the control of nausea and vomiting. Although perphenazine, like prochlorperazine, appears to have an over-all clinical toxicity somewhat less than that of chlorpromazine, physicians should be alert to the possibility of the development of jaundice, blood dyscrasias, or neurological sequelae referable to extrapyramidal involvement and should maintain close supervision of patients to avoid these complications.

Dosage.—Perphenazine is administered orally, intramuscularly, and, rarely, intravenously. For oral use in the management of mild anxiety and tension states or as an antiemetic, the dose for adults ranges from 2 to 4 mg. three or four times daily. Doses of 4 to 8 mg. three times daily by mouth are suggested for ambulatory patients with psychoneurosis. For the treatment of institutionalized patients with psychosis, the total oral dose for adults ranges from 16 to 64 mg. per day given in two to four divided doses. The usual oral dosage for children between 1 and 6 years of age is 2 mg. two or three times daily; for children between the ages of 6 and 12 years, the oral dose is 2 mg. three or four times a day. A total daily oral dose of more than 12 mg. is seldom necessary to elicit a favorable response in children.

Perphenazine may be injected intramuscularly when rapid effect or prompt control of an acute or intractable situation is required or when oral therapy is not feasible. The usual initial dose is 5 mg. This may be repeated every six hours. The total daily dosage usually should not exceed 15 mg. in ambulatory patients or 30 mg. in hospitalized patients. Oral therapy should be substituted as soon as practicable.

Intravenous administration of perphenazine is not recommended except when absolutely necessary to control severe vomiting, intractable hiccoughs, or acute symptoms, such as violent retching during surgery. When indicated, the drug should be administered at a rate not to exceed 1 mg. per minute, and the total intravenous dose should not exceed 5 mg. The drug is preferably given diluted in isotonic sodium chloride solution, with use of either fractional injection or slow drip infusion.

By all routes of administration, the lower range of adult dosage may be used in children over 12 years of age.

Preparations: solution (injection) 5 mg. in 1 cc.; syrup 0.4 mg. in 1 cc.; tablets 2, 4, 8, and 16 mg.

Applicable commercial name: Trilafon.

Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of perphenazine.

TUBERCULOUS MENINGITIS.—Tuberculous meningitis is now a curable disease. This became possible for the first time in 1947, with the advent of streptomycin. From 1947 to 1952 the survival rate in the Children's Medical Service of the Bellevue Hospital was maintained at over 60 per cent using streptomycin and Promizole. After 1952, when isoniayid became available, the numbers of survivors increased everywhere. At the present time the survival rate is reported to be from 60 to 95 per cent, depending upon the stage and duration of the disease at the onset of therapy. . . . During the early phase of tuberculous meningitis there occurs a hypersecretion of cerebrospinal fluid with distention of the cisterns and cerebral sulci. This facilitates the passage of air with unusually good filling on encephalography. In a few patients the third ventricle may be distended sufficiently to cause a physiological block of the basilar cisterns. This can be determined by cisternography. . . . Although the patient may appear critically ill, the patency of the basilar system favors a good prognosis. . . . Pneumoencephalography should be performed in children with tuberculous meningitis when the progress, clinical or chemical, is unsatisfactory. The procedure is of great importance in evaluating the underlying pathological process and any modification in therapy. The presence of obstruction in the basilar cisterns usually indicates a poor prognosis. In a few cases arrest of the hydrocephalus will occur spontaneously. Patients in whom the meningitis is arrested, but in whom the hydrocephalus is progressive, become problems of surgical management. A normal pneumoencephalogram usually, but not always, indicates a good prognosis.—J. E. Sifontes, M.D., S. V. R. Sordillo, M.D., and E. M. Lincoln, M.D., Pneumoencephalography in Tuberculosis Meningitis, *The Journal of Pediatrics*, June, 1957.

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SCIENTIFIC PROGRAM AT SAN FRANCISCO MEETING

SEVERAL sections of the Scientific Assembly of the American Medical Association will soon be celebrating centennial observances. These sections, originating in 1859, were conducted as a group of special medical organizations at A. M. A. meetings for many years and often were the only specialty groups in existence. For instance, the Section on Surgery carried on its program for more than half a century before the American College of Surgeons was founded. The programs consisted largely of essay types of presentations, and there was little or no coordination between sections. Each section made up its own program independently and published its own volume of proceedings.

The first meeting of section secretaries took place in 1913, at which time emphasis was placed upon better coordination of subjects among the various sections. In 1914, the Council on Scientific Assembly was established to assist section secretaries in this endeavor. For many years, however, the Council on Scientific Assembly and the Committee on Scientific Exhibit (which dated from 1899) worked independently, both producing programs to compete for the attention of the same audience. It was not until 1953 that the Council on Scientific Assembly and the Committee on Scientific Exhibit were combined into one group.

The type of medical meeting has changed markedly with these improvements, with fewer and fewer of the essay type of presentation and more and more of other means of medical communication. The Scientific Exhibit was started in 1899, medical motion pictures appeared on the program about 1914 and television in 1948. Thus, from the experience of many years, the program at the San Francisco meeting will be outstanding, attracting the specialist as well as the physician in general practice.

Headquarters for scientific activities at San Francisco will center in the Civic Auditorium, where all activities will be held on Monday and on Tuesday morning. The Scientific Exhibit begins at 8:30 Monday morning, with some 300 exhibits covering the various phases of medicine, and will continue to Friday noon. Outstanding demonstrators will be on duty to answer questions and discuss problems with visiting physicians. Among the features of the Scientific Exhibit will be the Special Exhibit on Fractures, with the leading surgeons of the United States in attendance. The Fresh Tissue Pathology Exhibit will be presented under the auspices of the Section on Pathology and Physiology and includes a long list of guest demonstrators from leading medical schools. Perinatal problems with demonstrations on resuscitation of the newborn infant will be presented under the auspices of the Sections on Obstetrics and Gynecology, Pediatrics, and Anesthesiology. Physical examinations of physicians will be conducted under the auspices of the Section on General Practice, assisted by competent cardiologists and radiologists. A question and answer conference on nutrition will be conducted with the cooperation of the Council on Foods and Nutrition of the American Medical Association.

The General Scientific Program of lectures will start Monday afternoon with a symposium, "The Care of the Severely Injured Patient." On Tuesday morning, the subject will be "The Hazards Associated with Therapeutic Agents."

The 21 sections of the Scientific Assembly will start their meetings Tuesday afternoon and continue through Friday noon. Many of the sections will hold joint sessions with each other, thus emphasizing the interdependence of one branch of medicine upon another. Panel discussions and symposiums will be featured with audience participation as much as possible.

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Color television will originate in San Francisco Hospital and will carry the operating room directly into the meeting hall at Civic Auditorium. Sessions will be held each morning and afternoon throughout the week, showing material that would not otherwise be included in the Scientific Program. Meanwhile, the motion picture program will show the latest advancements of medicine in the United States, as well as elsewhere, with a carefully arranged schedule of films selected for their general interest.

The high caliber of the program in San Francisco is indicated by the fact that the armed forces will give credit for training to reserve officers who attend the meeting, while the Academy of General Practice will give credit in category I for academy members. Any physician who is fortunate enough to attend the meeting in San Francisco will be well repaid for his effort.

GLAUCOMA

It is estimated that over one million persons in the United States have undiagnosed glaucoma.[1] This is about 2% of all persons over 40. The number of cases in persons under 40 is negligible, but the incidence increases rapidly with increasing age. Because we have an aging population, because glaucoma is a leading cause of blindness acquired after 40, and because early recognition is essential if blindness from this cause is to be prevented, screening programs are being used on an ever-increasing scale. The disease is insidious in that there is usually no pain and the progressive narrowing of the visual fields is not appreciated by the victim until it is far advanced. We are here referring to chronic simple or open-angle glaucoma, which is the commonest type.

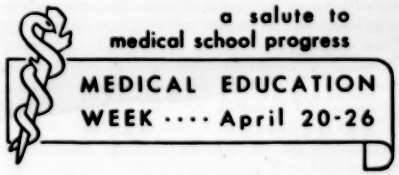
Since there are not enough trained ophthalmologists to screen the entire population over 40, it has been necessary to devise a relatively simple means of discovering those who may have glaucoma. Such an examination may include a brief history (including family history), a test for visual acuity, an estimate of the intraocular pressure, and the use of an ophthalmoscope. Suspected cases can be further screened by mapping the visual fields. All of these measures can be done by general practitioners and suspected cases referred to an ophthalmologist for provocative tests and a definitive diagnosis. Those whose tests are negative should be urged to have a recheck at least every two years after 40. "Glaucoma days" have been organized in several communities in California.[2] Advance notices are sent to all churches, to be read from the pulpit, and spot announcements are made over radio and television. Follow-up of suspected cases is essential. In 11 glaucoma-day drives in California, 12% of those screened were referred to an ophthalmologist and 3.7% were found to have glaucoma. An unexpected benefit of these campaigns was that a large number of persons who did not attend the screening examination later went to an ophthalmologist for a check-up as a result of the publicity accorded the subject.

It has been amply demonstrated that the general practitioner can play an important role in the early detection of glaucoma. Although we were all taught to estimate intraocular tension by finger pressure on the closed lids, this method is extremely unreliable. Proper use of a tonometer is no more difficult than the use of the sphygmomanometer and, if anything, is more important. Horsley and co-workers (page 1265 this issue) urge that taking the ocular tension with a tonometer be made a part of every general physical examination in patients over 40 whether in the office or on admission to the hospital. It should also be a part of insurance examinations and preemployment examinations in all persons in this age group. When this is done community glaucoma surveys will no longer be necessary.[3] Another important point in the prevention of glaucoma is brought out in the timely paper by Cholst and co-workers (page 1276, this issue).

1. Kurland, L. T., and Taub, R. G.: The Frequency of Glaucoma in a Small Urban Community, Am. J. Ophth. 42: 539-544 (April) 1957.

2. Gradle, A. H., and Downing, B.: Community-wide Glaucoma Case Finding, Sight-Saving Rev. 27: 78-82 (Summer) 1957.

3. Vaughan, D. G., Jr., and others: Glaucoma Detection, Sight-Saving Rev. 27: 145-148 (Fall) 1957.



ORGANIZATION SECTION

STATEMENT SUBMITTED TO WAYS AND MEANS COMMITTEE BY THE A. M. A., CONCERNING H. R. 9 AND H. R. 10

The American Medical Association would like to take this opportunity to submit, for the consideration of the Ways and Means Committee, views concerning H. R. 9 and H. R. 10, 85th Congress, currently being studied by your Committee.

The American Medical Association vigorously endorses the principle of these bills, which are measures designed to provide tax deferment on retirement funds for self-employed persons. The American Medical Association has endorsed the principle of legislation of this type for a number of years. We have collaborated closely with representatives of the American Bar Association, the original sponsors of this measure, and other national organizations of self-employed taxpayers who would be afforded some measure of tax equity by the enactment of these bills.

Early in 1948, our Board of Trustees was apprised of a movement to promote enactment of federal legislation under which self-employed persons could finance their own retirement plans through the deduction of amounts from their taxable income. Our Board approved this movement, which action was endorsed by our House of Delegates, the governing body of the Association, at its meeting in June, 1948.

On May 13, 1952, representatives of the Association appeared before your Committee in general support of H. R. 4371 and H. R. 4373, 82nd Congress. At that time, we suggested various amendments to those bills. H. R. 9 and H. R. 10 now before your Committee include all of the basic amendments recommended by the Association in 1952.

On Aug. 12, 1953, representatives of the Association again appeared before the Committee in support of H. R. 10 and H. R. 11, 83rd Congress.

It is the belief of the American Medical Association that physicians, dentists, veterinarians, lawyers, farmers, small businessmen, and the many others who comprise the nation's self-employed have long been neglected in federal tax legislation relating to pensions. Under the existing law, corporations are entitled to set aside tax-free money to purchase pensions and annuities for their employees, and millions of employees are benefiting from that arrangement. Yet the self-employed are denied this tax advantage in providing for their old age. The purpose of these bills is to eliminate this discrimination and inequity. By extending the tax deferment privilege to the country's 10 million self-employed, this legislation will give them an increased incentive during their best earning years to save for their old age.

Unless something is done to make self-employment as financially attractive as the employee relationship, we believe there is a grave danger that many professional men will bypass the private practice of their profession. The trend today is definitely toward becoming an employed person. This situation also contributes to a maldistribution of physicians since it makes the large city more attractive to the young professional man by providing more opportunities for him to become employed.

On the basis of our observations over many years, we are convinced that this is one of the factors contributing to the pronounced migration of professional people into urban areas. So, quite apart from the objective of obtaining tax equality with our employed counterparts, we urge you to approve legislation of this type, because it is in the public interest.

This legislation will be of particular benefit to physicians and other professional men who go through a long and costly period of training, and whose earnings are bunched into a comparatively few years when they are subject to high income tax rates.

Under the program proposed in the pending bills, the amount of each person's pension would be determined by his own contributions, without one cent being added by the government. In addition, the program would not force an individual into idle retirement in order to draw upon his pension fund. Most important, it presents an opportunity for all who can provide for their own retirement to do so without undue discrimination against those who work for themselves.

These comments indicate very briefly the general viewpoint of the American Medical Association toward this legislation. Because it removes a discriminatory factor which now discourages the private practice of medicine and other professions, it is in the public interest. Because it relieves an existing inequality, it should commend itself to you. Our Association is glad to join the other great national organizations of the self-employed in urging that your Committee act favorably on these bills.

SUMMARY OF CONGRESS ON MEDICAL EDUCATION AND LICENSURE

For the first time in 54 years the Annual Congress on Medical Education and Licensure has called heavily upon leaders outside of medicine as key program participants. Twenty-nine men prominent in sociology, industry, economics, business, labor, agriculture, political science, higher education, insurance, government, and philanthropy joined with several dozen medical leaders on Feb. 8 through 11 to explore and report on the Congress theme: "Challenges in Medical Education—Focus on Future Needs."

More than 1,000 medical educators attended these sessions sponsored by the A. M. A. Council on Medical Education and Hospitals, in cooperation with the Advisory Board of Medical Specialties and the Federation of State Medical Boards of the United States. Following are highlight excerpts from individual papers, panel discussions, and workshop summary reports (detailed presentations will appear in one or more future issues of THE JOURNAL).

Population Characteristics and Trends

The growing mobility of our population will create at least one problem for physicians, according to Dudley Kirk, demographic director of Population Council, Inc. He said: "The classic situation of the family doctor who knows the medical history of his patients by virtue of having treated them from birth seems on the way to complete disappearance. Increasingly, physicians will be faced with the problem of dealing with a segment of a person's life."

Regarding practice prospects, Kirk noted that "if it is still good advice to recommend that the young man starting his career 'go West,' it is even better advice to the young doctor to recommend that he set up practice or join a medical center in the suburbs. . . . Obstetricians and pediatricians are likely to continue to be in demand, and the growing need for specialists in degenerative diseases and geriatrics seems likely to persist." At the same time he noted: "Not many of you may realize that the number of foreign physicians undergoing graduate training in the United States is about equal to the number of all medical students who graduated in the U. S. last year. But we can anticipate a growing supply of medical school candidates in the future."

In an ensuing workshop on population, participants reported "a strong trend toward group practice which may result in providing better service around the clock yet fewer work hours per week by the average member of the group." They also reached the conclusion that demands for medical service "have been about in equilibrium" with the supply of physicians, "but we have no reliable data on which to base an estimate of the need."

Changing Society

The medical profession, said Harvard sociology professor, Talcott Parsons, "must learn to cooperate with many different lay agencies, starting with the sciences which are not as such primarily medical." He predicted that medicine will eventually have two great primary branches—"psychological medicine" and "somatic medicine." If the profession does not meet the "enormous demand for services from psychiatrists" other agencies will step in, according to Professor Parsons. He said: "I do not look for what has usually been meant by 'socialized medicine' in the future in this country, nor do I look for preservation or restoration of the pattern where the typical physician practiced on a strict fee-for-service basis. There will not be less, but more collective organization."

Dr. Parsons also took part in a workshop session which concluded that the four most significant sociological trends affecting medical education are emphasis on industrialization, suburbanization, the "migratory manner of American life," and early marriage. Workshop participants also agreed that if health insurance programs are to survive "we believe they need to be re-evaluated—casualty type policies will need to replace prepayment plans. If they do not, costs will continue to soar."

The workshop summary report stated: "There are very few determined to die just to cash in on their life insurance premiums; there are very few who deliberately seek accidents to cash in on their automobile collision policies; there are very few who burn down their homes in order to 'get their money's worth' out of fire insurance. Yet the majority of policy holders appear determined to cash in every year on their health insurance." The workshop also touched on the following topics.

Private Patients for Teaching: "There is nothing educationally unsound in the use of intelligent, paying, private patients for teaching purposes. They have common ills, and they are the obvious type of patient for whom the student will be largely responsible in his active professional career. The implications of these patients as the predominant source of teaching material poses real problems, however, in graduate medical education."

Family Physicians: "The movement to suburbanization and the increasing number of young families will lead to a greater need for family physicians in contrast to specialists in narrow fields. . . . We pictured him as clinic oriented, calling upon consultants in urban medical centers. . . . This physician would be community-related, that is to say one who played a prominent role in community life. We look upon him as a well-rounded physician aware as well of social change as of medical prog-

ress. . . . Society, we feel, will want the physician to be a professional man of great skill, intelligent and wise, forbearing and forgiving, gentle and kind, a family man but willing to leave his home at another's will, as well as to be a civic leader. . . . No other profession—one that has given so much and promises to give even more—is as profoundly introspective as medicine, so close to being masochistic."

Population Ratio: "We are not convinced that anyone knows (or ever will) if there is an optimal ratio of physicians to population. We are convinced that a reporting of such a finite figure can be harmful to medicine. It is fairly obvious that this figure must vary with types of population as well as with availability of paramedical personnel."

Economy Characteristics

An important force in changing characteristics of our economy, as it affects medical education, is the growth of government, according to Meyer Kestnbaum, president of the Hart Schaffner and Marx clothing firm. Kestnbaum, who has been active in Presidential advisory groups dealing with economic questions, said: "It is amazing how many people still believe that government services are free."

Workshop participants reported: "As government is the fastest growing business in society it has great potential effect in medicine. Fifteen percent of all hospital beds belong to federal agencies—are they put to the best use for medical education? The workshop doubted it." The conferees also agreed that a large part of the share of the cost of medical education today is borne by indirect federal subsidy and that continuing subsidy would be unwise because of the inherent dangers of "federal control." How can increased medical education costs be met? The workshop participants suggested that tuition should be increased to "more realistic figures" to cover a larger percentage of the total cost. They stated: "It was agreed that higher tuition figures would not impose an undue burden on many families and students. However, scholarships should be sufficient in amount to cover higher tuition for those students who are in need of help."

Dimensions of Knowledge

Medical knowledge is changing in so many dimensions, according to Dr. Hugh H. Hussey Jr., that the physician's most serious difficulty is in staying abreast of it all. Dr. Hussey, an A. M. A. Trustee, who is professor of medicine at Georgetown University School of Medicine, said: "Better means must be devised for his postgraduate education if he is to assimilate all he should.

"Please understand," he added, "that I believe in medical research as an integral part of medical education. However, there are threats of danger when medical schools make a fetish of research, when it derives much of its financial support from sources that in turn influence its direction, when it outweighs other considerations for academic advancement, and when it becomes the province of untrained or half-trained workers."

A workshop group on the topic of changing dimensions of medical knowledge reported: "It is deplored that there is a monotonous uniformity in the kind of educated individual who enters medical school. . . . Lip service is given by medical schools to the desirability of a broad general education and an avoidance of the requirement of excessive scientific premedical preparation." Regarding medical school curriculum, participants asked: "Should not the curriculum be modified on the basis not necessarily of the plans of the student for his future practice and life work but rather on the basis of his immediate interests, inclinations and curiosities? . . . Because medical practice will become more and more an enterprise of teams of physicians, might it not be feasible and desirable to eliminate significant masses of knowledge required at the present time of all medical students?"

Other Comments

Theodore O. Yntema, vice-president of the Ford Motor Company: "The teaching of calculus, diagnosis and basic principles of inventing and inventions should start in kindergarten—and I say that without the least intent at humor."

A. M. A. President David B. Allman: "Efforts to compare unqualified statistics for physician-population ratios in recent years with those early in the century is not only meaningless, but actually harmful."

Dr. Leland S. McKittrick, Chairman of the A. M. A. Council on Medical Education and Hospitals: "Are we giving proper consideration to the effect of our changing medical and socioeconomic conditions upon the training of our recent medical school graduates in preparation for their place in the community? Are we developing too many top flight generals able to care for the relatively few patients with complicated medical and surgical conditions and not enough foot soldiers trained to adequately care for the greater proportion of our population?"

Dr. Ward Darley, executive director of the Association of American Medical Colleges: "With medicine increasing in effectiveness, with our population growing in size and with our per capita level of education and purchasing power continuing to improve, we must anticipate the narrowing of the gap between medical need and demand and between medical knowledge and practice."

Dr. Allan C. Barnes, chairman of the department of obstetrics and gynecology at Western Reserve University School of Medicine: "Medical insurance

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companies must be re-educated to recompense for the care rendered by the resident group. I live in a state which does not require an internship prior to practice. Therefore a man who graduated from medical school last year and is practicing this year may collect from Blue Shield in Ohio for a hysterectomy, no matter how well indicated or how completely executed. On the other hand, a man with an internship, a year of training in general surgery, and three and a half years of thorough specialized training in obstetrics and gynecology cannot collect insurance for a hysterectomy because he bears the title of resident."

Dr. L. T. Coggeshall, president of the Association of American Medical Colleges: "The more medicine we practice and the more people benefiting from that practice, the greater will be the public appetite for medical service."

Dr. C. J. Gaspel, president of the Federation of State Medical Boards of the United States: "While the incidence of addicts in the general population is one addict to every 3,000 people, among physicians it is one addict to every 100 people or 30 times more prevalent. . . . Medical curriculum should be revised so that more time is spent teaching students of the dangers and pitfalls they may face when they are permitted to have a narcotics license and thus have free access to dangerous drugs." (Dr. Gaspel said that some physicians become addicts by using narcotics to relieve liquor hangovers, by failing to stop using narcotics after administration during recovery from some painful disease, or by taking narcotics in an effort to relieve exhaustion.)

AMEF Grants

At the Congress, grants totaling $984,787 were presented to 85 medical schools by the American Medical Education Foundation. Said Dr. George F. Lull, president of the AMEF: "This represents only part of the generosity with which the physician supports his schools. He has also given substantially to his individual school in money and volunteer teaching time."

FEDERAL MEDICAL LEGISLATION

Second Session, 85th Congress

The President's budget message asking for an increase in defense appropriations and for a vast program to improve science teaching and to provide scholarships for capable students was no surprise. What was a surprise was his proposal to revise legislation affecting five of the grant-in-aid programs of the Health, Education, and Welfare Department which would bring about some small reduction in the 1959 budget and larger reductions in later years, as was the administration's proposal that the 12-year-old Hill-Burton Hospital Construction Program be curtailed after June 30, 1959, the date the present act expires.

The President stated: "I am also making recommendations to reduce some programs, to curtail expansion in others and to transfer greater responsibility from the Federal government to state and local governments or to private individuals or enterprises. All of these recommendations, in addition to being required by sound public policy, will help to hold expenditures in future years to prudent levels. . . . As I have repeatedly emphasized, the continued vitality of our Federal form of government requires that, to the maximum extent possible, primary responsibility for public programs be shouldered by that level of government most familiar with local problems and most responsive to them. We must exercise the utmost restraint in assigning new programs and responsibilities to the Federal government, and we should continuously search out those programs and activities now carried on at the national level that can and should be handled by the states or localities." Following are analyses of some of the new bills.

Tax Deductions for Medical Expenses

H. R. 9633, introduced by Representative Boggs (D., La.) is similar to H. R. 9417 by Representative Miller (R., Md.). The bill would liberalize tax deductions for medical expenses incurred by a disabled individual over 65 years of age and for his spouse if also over 65 and disabled, not to exceed $20,000 in any one year. Sixteen previous bills to broaden tax credits for medical expenses were introduced in the first session of this Congress.

Tax Deduction for Education

H. R. 9971 introduced by Representative Ikard (D., Texas), similar to S. 2938 by Senator Frear (D., Del.), H. R. 10026 by Representative Sikes (D., Fla.), and H. R. 10030 by Representative Teller (D., N. Y.), would provide an additional exemption of $600 for each individual attending an educational institution above the secondary level. Some bills would include the taxpayer and his dependents, others only dependents. (Twenty-eight bills to give varying degrees of tax reduction for educational expenses were introduced in the first session.)

Social Security

A number of measures affecting Social Security have been introduced. One by Representative Roosevelt (D., Calif.), H. R. 9835, would put all self-employed physicians under compulsory Social Security coverage beginning with the taxable year 1958. Another Roosevelt bill, H. R. 9834, would

From the Washington Office of the American Medical Association.

increase in 1959 the wage base on which Social Security taxes are paid under the Old Age and Survivors Insurance Program from the present base of $4,200 to $10,000 and would also provide an increase of $500 for each year the Consumer Price Index rose five points. If enacted, an individual with an income of $10,000 per year would receive monthly benefits of $225, and the same individual, by 1975, if self-employed, would be paying at least $637.50 per year to the fund.

H. R. 9836 by Representative Roosevelt would legalize the requirements for eligibility for disability benefits of an individual if he were over 50 years of age, were fully or currently insured, and could not obtain employment in an occupation similar to that prior to his disability, because of said disability. H. R. 10002 by Representative Fino (R., N. Y.) is similar to that of Representative Roosevelt, H. R. 9834, but would only raise the base wage to $6,000 and increase the benefits to $138.50 a month. The individual Social Security tax would be increased to about $387.50 per year, by 1975, for the self-employed.

Veterans Legislation

Representative Teague (D., Texas), in H. R. 9700, has undertaken a monumental task of consolidating all the laws administered by the Veterans Administration into a special act. H. R. 9717, similar to H. R. 917, by Representative Rogers (R., Mass.) is similar also to H. R. 1264 by Representative Shuford (D., N. C.), H. R. 2431 by Representative Fino (R., N. Y.), and H. R. 3821 by Representative Christopher (D., Mo.). They provide that certain veterans with active pulmonary tuberculosis are regarded as permanently and totally disabled for pension purposes while hospitalized. H. R. 9726 by Representative Smith (D., Mass.) would make permanent any service-connected disability for which the veteran has been receiving compensation for 10 or more years, even if the disability has been rehabilitated. It would also provide that, if prior to passage of the bill any disability was held to be service-connected for a period of 10 years or more and subsequently held to be non-service-connected, the veteran or his dependents could make application for a service-connected disability and receive all benefits provided by law.

H. R. 9896 by Representative Aspinall (D., Col.), similar to H. R. 929 by Representative Rogers (R., Mass.) would lengthen the presumption of service connection from two to three years for multiple sclerosis and chronic functional psychosis developing to 10% disability.

H. R. 10028 by Representative Teague (D., Texas) would provide that no VA Hospital, domiciliary, medical center, or regional office could be closed or transferred unless the House Veterans Affairs Committee (of which Representative Teague is chairman) was notified 90 days in advance of the proposed closing or transferring; if Congress ended a session prior to the 90-day period or was not in session, the facility could not be closed. Representative Teague, in H. R. 10029, would increase the presumption of service connection for organic heart disease, 10% disability, from one-to-two years.

Old-Age Problems

Representative Fogarty (D., R. I.), in H. R. 9822, similar to S. 2994 by Senators Neuberger (D., Ore.) and Kefauver (D., Tenn.), calls for a White House Conference on Aging prior to the end of 1958. It would also assist the states in conducting similar conferences on aging prior to the White House Conference.

Welfare and Benefit Plans

Senator Mundt (R., S. D.), in S. 3044, would change the National Labor Relations Act so as to provide safeguards against the misuse of funds of labor organizations set aside for union welfare and benefit plans, including health plans. The labor organizations would be required to have a certificate on file with the Comptroller of Currency in the Treasury Department showing that books and records of the international union organization and those of the welfare plan had been examined by the comptroller. The comptroller would be required to ascertain if the welfare funds have been invested in securities in which a national banking association is prohibited from investing in. If such is the case, or if the funds are not being administered for the purpose for which they are collected, he is to notify the labor union officials. If the practice is not promptly discontinued, the comptroller is authorized to publish a report of such practices. If, in his opinion, the practices constitute a violation of law, he is required to make the facts known to the appropriate enforcement officers. The bill would further remove the tax exemption of any labor union not meeting its provisions. Further, any union employee found guilty of embezzling welfare funds or benefit funds is made subject to a fine of $5,000 or five years imprisonment, or both.

Miscellaneous

Representative Burdick (R., N. D.), in H. R. 10096, would prohibit any officer of the United States or territories, or the District of Columbia from treating any water for human consumption with fluoride compound.

MEDICAL NEWS

ALABAMA

Dedicate Medical Library at Birmingham.—The Lawrence Reynolds Library was dedicated at the University of Alabama Medical Center, Birmingham, Feb. 2. Presentation of the collection of rare books and other historical medical items was made by the donor, Dr. Lawrence Reynolds, a native of Alabama now residing in Detroit. Dr. Frank A. Rose Jr., president of the university, accepted the collection on behalf of the Medical College. Dr. Merrill C. Sosman, professor emeritus of Harvard University, gave the principal address. The Reynolds collection has been assembled over the past four decades from all sections of the world. Included are items from the Dr. Arno B. Luckhardt and Daniel Drake collections and original Pasteur letters. There are over 5,000 volumes. The Reynolds Library is the first unit of a proposed million-dollar library which will serve the entire Medical Center.

ILLINOIS

Chicago

Dr. Lobitz to Give the Pusey Lecture.—The Pusey Lecture of the Chicago Dermatological Society will be given by Dr. Walter C. Lobitz Jr., of Hanover, N. H., at the Illini Union March 19. The title of the lecture will be "An Anecdote of an Agnostic Allergist."

Hospital News.—Dr. Arthur A. Rodriquez has been appointed physiatrist and director of physical medicine and rehabilitation at the Salvation Army, Catherine Booth Hospital and Clinics. Extensive expansion of the physical medicine and rehabilitation section is planned.

Conference on Cardiovascular Advances.—The Cardiovascular Committee of the Cook County Hospital has announced a special cardiac conference for March 22, 3-4 p. m., in the Children's Amphitheater of the hospital. The subject will be "Recent Advances in Some Types of Cardiovascular Diseases." The guest speaker will be Dr. Paul H. Wood, director, Institute of Cardiology, London, England. Participants include Drs. S. Howard Armstrong Jr., Louis Feldman, Egbert H. Fell, Don C. Sutton, and Benjamin M. Gasul, chairman. Physicians are invited. For information write Dr. Benjamin M. Gasul, Cook County Children's Hospital, 700 S. Wood St., Chicago 11.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

KANSAS

Physicians Meeting in Emporia.—The Kansas regional meeting of the American College of Physicians will be held March 21 at the Broadview Hotel, Emporia. The program includes the following papers:

Experience with Porphyria in Private Practice, Dr. William T. Sirridge, Kansas City.
Serum Proteins in Chronic Lymphatic Leukemia, Drs. Robert P. Hudson and Sloan J. Wilson, Kansas City.
Clinical Implications of Some Aspects of Liver Biochemistry, Dr. Robert T. Manning, Kansas City.
Repair of Coarctation of the Aorta in a 60 Year Old Hypogonadal Male, Dr. Chiung-Ming Chen, Kansas City.
Nothnagel's Syndrome, Dr. Lew W. Purinton, Wichita.
Philosophy of Rehabilitation in Chronic Disease, Dr. Herschel A. Flanders, Hays.
Treatment of Cushings Syndrome with Amphenone, Dr. Harvey A. Tretbar, Wichita.
Enzymes in Myocardial Infarction, Dr. George L. Norris, Winfield.
Transaminases in Serum and Liver Correlated with Liver Necrosis, Dr. Samuel Zelman, Topeka.

Dr. Philip S. Hench, Rochester, Minn., regent of the college, will be guest speaker at the dinner. For information write Dr. John L. Kleinbeksel, Chairman, Program Committee, American College of Physicians, 3244 E. Douglas Ave., Wichita 8, Kan.

MISSOURI

Hospital Alumni Meeting.—The St. Louis City Hospital Alumni Association will hold its 70th annual meeting April 14 at the Le Chateau Restaurant at 10405 Clayton Road, St. Louis County. The Missouri State Medical Association will be meeting in St. Louis at the same time. Dr. Robert Koch is the president for this year. For information write Dr. Drennan Bailey, Missouri Theatre Building, 634 N. Grand, Room 1114, St. Louis 3.

NEW JERSEY

Society News.—The following officers of the New Jersey State Society of Anesthesiologists, have been installed: president, Dr. Charles H. Hall, Upper Montclair; vice-president, Dr. Genesio L. D'Allesandro, Glen Ridge; treasurer, Dr. George T. Henderson, Bound Brook; and secretary, Dr. David Fant, Ridgewood.—The annual dinner meeting of the New Jersey Gastroenterological Society will be held

April 9 at the Essex House in Newark. The scientific session will be devoted to a symposium on "Inflammatory Diseases of the Esophagus and Their Treatment." Drs. John H. Garlock, surgeon, Bernard S. Wolf, radiologist, Max L. Som, endoscopist, Asher Winkelstein, gastroenterologist, all of Mt. Sinai Hospital, New York City, will be the speakers.

NEW MEXICO

Poison Information Center.—The New Mexico Pharmaceutical Association announces the opening of a Poison Information Center at the Bernalillo County–Indian Hospital Emergency Room, Albuquerque. The service at this center is available to all physicians in the state. The center is designed to aid the medical profession in determining the poisonous ingredient in plants and chemical preparations and is stocked with books on plants, listings of preparations, and treatment of various types of poisoning.

NEW YORK

Industrial Accidents in 1957.—An 11-year record low of 718,874 industrial accidents in New York State were reported to the Workmen's Compensation Board last year. The number represented a decrease of 4% from the 748,860 reported in 1956 and was only 409 above the postwar low of 718,465 in 1946. After reaching an all-time peak of 861,845 accidents reported in 1951, a steady decline followed, resulting in a decrease of 16.6% from 1951 to 1957. Accidents which required indexing of claims and hearings totaled 180,431 last year, a drop of 1.2% from the 182,662 cases indexed in 1956.

Open Third Unit for Geriatric Mental Patients.—The third intensive treatment unit for newly admitted geriatric patients organized by the New York State Department of Mental Hygiene has been opened recently at Hudson River State Hospital, Poughkeepsie. The unit is designed to treat patients with psychiatric conditions who are over the age of 65. The two other units were set up in 1956 at Central Islip and Buffalo state hospitals. The Hudson River unit, located in the Cheney Memorial Building, has two wards, one for each sex, with a total of 60 beds. Rooms for physiotherapy and occupational therapy are available. Dr. Peter L. Goode, supervising psychiatrist, is in charge of the new unit.

University News.—Dr. Manuel René Malinow, chief of research, Institute of Physiology, University of Buenos Aires Medical School, Argentina, presented "Mechanisms Involved in the Pathogenesis of Atherosclerosis" Jan. 16 as a Harrington Lecture sponsored by The University of Buffalo School of Medicine.——The Tau Chapter of the Phi Delta Epsilon Fraternity at Syracuse University College of Medicine will hold its annual lecture March 26, 8:15 p. m., in the auditorium of the Medical College Building. The guest speaker will be Dr. William Dameshek, of the New England Center Hospital, Boston, who will discuss "Polycythemia Vera and Related States."

New York City

Appoint Dr. Nagamatsu Department Director.—Dr. George R. Nagamatsu has been appointed director of the department of urology at New York Medical College, Flower and Fifth Avenue Hospitals, where for the past 15 years he has been a faculty member. He is a diplomate of the American Board of Urology, a fellow of the American College of Surgeons and the New York Academy of Medicine, and a member of the New York Urological Society and the American Urological Association.

Personal.—Dr. Bernard L. Pacella has been presented with the "Cavaliere, Ufficiale 'nell Ordine al Merito della Republica," an Italian government decoration.——Dr. Harry A. Solomon, director of medical services at Beth David Hospital, was presented a symbolic key recently at the dedication of research laboratories in his honor as a citation for 40 years of medical practice and research.——Dr. Goodwin M. Breinin has been appointed to the first Daniel B. Kirby professorship of research ophthalmology in the department of ophthalmology, New York University–Bellevue Medical Center. Dr. Kirby was professor of ophthalmology at New York University from 1940 to 1949 and emeritus professor until his death in 1953. Dr. Breinin is at present director of research in the department of ophthalmology at the New York University Post-Graduate Medical School, a position which he will continue to fill.

Research Fellowship in Ophthalmology.—The department of ophthalmology of the New York University–Bellevue Medical Center announces establishment of the Daniel B. Kirby fellowship for research in ophthalmology. To be eligible a candidate must have had a "thorough grounding" in ophthalmology, equivalent to a three-year residency, or should have acquired "equivalent competence in a basic field related to ophthalmology." Fellows will be expected to continue work on basic problems in such fields as ocular chemistry, physiology, pathology, or experimental surgery, and will be supplied laboratory space and facilities in the center. The initial appointment will be for one year at a basic stipend of $7,000 and will be subject to renewal for two additional years. Dr. Kirby, who died in 1953, established the Eye Surgery Fund to which Mrs. Charles Melbourne Higgins subsequently contributed additional funds in honor of her husband. Application should be submitted

before May 1 to the Dean, New York University–Bellevue Medical Center, 550 First Ave., New York 16.

NORTH CAROLINA

University Grants.—A senior research fellowship grant of $61,560 from the U. S. Public Health Service has been made to Dr. John K. Spitznagel of the department of bacteriology and immunology of the University of North Carolina Schools of Dentistry and Medicine, Chapel Hill, to cover a five-year study of "Metabolic Aspects of Bacterial Ecology in Host Tissues." This is the fourth Senior Research Fellowship to be awarded to faculty members in the School of Medicine within a year by the Public Health Service. The other three grants, totaling $164,000, went to Dr. Robert D. Langdell, assistant professor of pathology; Billy Baggett, Ph.D., assistant professor of pharmacology; and Ira Fowler, Ph.D., assistant professor of anatomy. During 1952-53 Dr. Spitznagel was a visiting investigator with Rene J. Dubos, Ph.D., of the Rockefeller Institute for Medical Research in New York City. Prior to joining the University faculty this past fall, he was chief of medical service at the U. S. Army Hospital, Fort Bragg.

OHIO

Law–Medicine Institute.—Western Reserve University's Law–Medicine Center has scheduled the fourth in a series of institutes for April 25-26 on the university campus. Entitled "The Mind: A Law-Medicine Problem," the program will be held in the courtroom of the university's School of Law. Medical specialists will lecture on "Personality Growth and Development: Childhood, Adolescence, Adult"; "Causes of Mental Diseases and Illnesses: Physical and Emotional, Precipitating and Predisposing"; "Management of the Traumatically Disabled Mentally Ill"; "Classification of Mental Diseases and Illnesses"; "Psychological Testing and Interviewing"; and "Law–Medicine Cases Involving Mental Diseases and Illnesses." Cooperating with the program will be the Cuyahoga County Coroner's Office, co-sponsor of the Law–Medicine Center. Tuition is $25. For information write Mr. Oliver C. Schroeder Jr., director, Law–Medicine Center, Western Reserve University, Cleveland 6.

PENNSYLVANIA

Philadelphia

Appoint Full-Time Professor of Surgery.—The appointment of Dr. John Malone Howard as head of the department of surgery at Hahnemann Medical College has been announced. Dr. Howard will replace Dr. William L. Martin who retires at the close of the 1958 academic year. Dr. Howard will become Hahnemann's first full-time professor of surgery. He became chief resident and fellow of the American Cancer Society in 1949 at the Hospital of the University of Pennsylvania. From 1945 through 1950, he was a member of the Harrison Department of Surgical Research at the hospital. He then became instructor in surgery at Baylor University College of Medicine, Houston, Texas, and in 1951 became assistant professor of surgery. From 1955 until his appointment at Hahnemann, Dr. Howard was Joseph Brown Whitehead Professor of Surgery and chairman of the department of surgery at Emory University School of Medicine, Atlanta, Ga. He was director from 1951 to 1953 of a surgical research team in Korea for the U. S. Army and was awarded the Legion of Merit.

RHODE ISLAND

New Children's Unit at Rhode Island Hospital.—The new Crawford Allen Building in the Rhode Island Hospital was opened for patients Jan. 2. The 32-bed unit, built at a cost of $560,000, is the second step in the establishment of a children's medical center at the hospital and was designed for the care of children with long-term illnesses. It adjoins the Potter Memorial Building, a 75-bed wing which was built in 1941 for the care of children with acute conditions requiring hospitalization. The new unit has two dining rooms, recreation rooms, a schoolroom, kitchen, and a hobby room for handcrafts. It covers more than 12,000 square feet of space and is adjacent to the indoor swimming pool. The unit was dedicated Dec. 28, with Mr. Louis C. Gerry, president of the hospital, as principal speaker.

The Crawford Allen Building of the Rhode Island Hospital, Providence.

WISCONSIN

Conference on Cell Chemistry.—A Conference on the Chemical Organization of Cells will be held in Madison, Aug. 21-23. Participants will be authorities on anatomy, biochemistry, embryology, and pathology who will present correlated recent information about the cell in a series of formal presen-

tations. Inquiries should be addressed to Dr. Joseph J. Lalich, professor of pathology, University of Wisconsin, Madison 6, Wis. A limited number of travel stipends may become available later this spring. Information will be circularized to those who have already registered with Dr. Lalich for the conference.

Symposium on Genetics in Research.—The department of genetics in the College of Agriculture and the department of medical genetics in the Medical School, University of Wisconsin, Madison, are cosponsoring a "Symposium on Genetics in Medical Research" April 7-10. Financial support is being provided by a grant from the Heart Institute of the U. S. National Institutes of Health. Participants will include experts from England, Scotland, Sweden, France, Italy, and Japan. April 7 will be devoted to registration and informal discussions and the following three days to presentation and discussion of the nine major papers. Dr. John Z. Bowers, dean of the Medical School, is the symposium chairman. For information write Joshua Lederberg, Ph.D., Corresponding Secretary, Symposium on Genetics, University of Wisconsin, Department of Medical Genetics, Madison 6, Wis.

WYOMING

Appoint Director of Mental Health Division.—Dr. Jesse E. Simons has been appointed full-time psychiatrist-director of the Division of Mental Health for Wyoming. The division began operations in September, 1957, following the actions of the 34th state legislature in calling for development of full-time mental health activities. Dr. Simons, who will assume his new duties July 1, served with the U. S. Public Health Service in Texas during 1951 and 1952. He was in general practice at Monticello, Utah, until 1955, when he entered psychiatry training with the Veterans Administration at Fort Douglas, Utah, and at the Salt Lake County General Hospital.

ALASKA

Director of Mental Health Section.—Dr. John B. K. Smith has assumed the position of chief of the Alaska Department of Health mental health section which position has been open since the resignation of Dr. Oscar E. Hubbard in February, 1957. Dr. Smith served as consulting psychiatrist for the department's mental health clinics during September. He received his medical degree at Glasgow University and served a three-year residency in psychiatry at Dykebar Mental Hospital in Paisley, Scotland. He practiced in both England and Scotland before coming to the U. S. in 1952. Dr. Smith comes to Alaska from Trenton, N. J., where he has been director of professional education and assistant clinical director of the State Mental Hospital since January, 1955.

GENERAL

Eastern Radiological Society.—The first meeting of the newly incorporated Eastern Radiological Society will be held on May 5-8 at Mid-Pines Club, Southern Pines, N. C. Reservations should be made early with the hotel management. Information and application forms for membership in the society may be obtained from Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, president; Dr. George R. Krause, 10900 Carnegie Ave., Cleveland 6,. vice-president; or Dr. John D. Osmond, Jr., Euclid-Glenville Hospital, Cleveland 19, secretary-treasurer.

Ulcerative Colitis Foundation.—A new medical research foundation has been organized with the encouragement of the National Institute of Arthritis and Metabolic Diseases "to promote research in ulcerative colitis." Mr. Miles Fiterman, Minneapolis businessman who heads the foundation, said plans are to provide researchers with "continuing and guaranteed funds." He explained that one of the foundation's purposes is to "provide a climate for research that will attract outstanding men so that more progress may be made in solving the problems of ulcerative colitis." The foundation's medical advisory board includes Drs. Joseph B. Kirsner, Walter L. Palmer, Jacob A. Bargen, Julian M. Ruffin, Stewart G. Wolf Jr., and Owen H. Wagensteen.

Post-Convention Tour to Hawaii.—A trip to the Hawaiian Islands has been planned in connection with the annual meeting of the American Medical Association in San Francisco in June. The journey will be sponsored by the Illinois State Medical Society, but other physicians and their families are being invited to join the group. The party will fly from San Francisco the night of June 26 and arrive in Honolulu the following morning. Sightseeing tours are arranged, and physicians may attend the Hawaiian Summer Medical Conference in Honolulu July 1-3. The group will leave Honolulu July 5 and members will have the option of returning by air or on the air-conditioned S. S. Lurline. For information write the Illinois State Medical Society, 185 N. Wabash Ave., Room 1909, Chicago 1.

Request Residency Posts for Indian Students.—The Indian Medical Association requests offers from recognized hospitals for residency posts in all specialties for doctors from India (men and women) specially selected for graduate training in U. S. hospitals for the session beginning July 1. These doctors will have a "good command of English—spoken and written." The hospitals must be approved by the U. S. State Department for Exchange-Visitor Program. Interested hospitals are requested to communicate directly, by Air Mail, with the Honorary Secretary, Indian Medical Association, "Hanging Bridge," Daryaganj, Delhi -7,

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India, giving offers of posts, terms of appointment, etc., including maintenance, stipend, and the allotted number for the exchange program.

Meeting in Boston on Allergy.—The New England Society of Allergy will hold its annual meeting March 19 at the Longwood Towers, Boston. Drs. John. L. Fromer and Francis M. Rackemann will preside at the afternoon and evening sessions, respectively. The program includes the following:

Identification and Counting of Pollen; Boston Pollen Surveys, Dr. Ralph E. Wheeler, Boston.
Maine Pollen Surveys, Dr. Martyn A. Vickers, Bangor, Maine.
Pollen Filters, Dr. Francis H. Chafee, Providence, R. I.
Specific Treatment of Pollinosis, Conventional Therapy, Dr. Jeremiah E. Greene, Boston.
Specific Treatment of Pollinosis, Abbreviated Therapy, Dr. Rackemann.
Repository Treatment of Inhalant Allergy, Dr. Mary E. H. Loveless, New York City.
Management of Bronchial Asthma in Children, Dr. Robert Chobot, New York City.

For information write the New England Society of Allergy, 300 Longwood Ave., Boston.

Organize Automotive Medicine Association.—At a recent meeting in Chicago the American Association of Automotive Medicine was organized by a group interested in the medical aspects of automotive racing. Purpose of the organization is to conduct regular meetings and exchange ideas in order to "make automobile racing and eventually automobile driving safer." The members have had experience in organizing the medical-safety coverage of races in different parts of the U. S. The following officers were elected: president, Dr. Abraham J. Mirkin, Cumberland, Md.; secretary, Dr. Werner P. Pelz, Charles City, Iowa; directors, Drs. H. A. Fenner Jr., Hobbs, N. M., William J. Gibson, St. Augustine, Fla., John E. Knight, Newton Center, Mass., George G. Snively, Sacramento, Calif., and Thomas P. Waring, Savannah, Ga. Any physician who has experience with automotive racing may write to Dr. Pelz for further information.

Bahamas Medical Conference.—The fifth Bahamas Medical Conference will be held at the Dolphin Hotel in Nassau, Bahamas, April 1-12. Speakers include Drs. Ethan A. Brown, Boston; Helen F. Dunbar and Irving Hirshleifer, New York City; Ralph I. Fried and Irvine H. Page, Cleveland; Caroline B. Hunter, Carlos P. Lamar, Philipp R. Rezek, and Donald W. Smith, Miami; Eugene L. Jackson, Ph.D., Richmond; Brig. General Thomas W. Mattingly, Washington, D. C.; Raymond W. McNealy, Chicago; and John R. Wood, Tuckahoe, N. Y. A panel discussion, "The Surgical Treatment of Coronary Artery Disease," will be moderated by Dr. John M. Chamberlain, New York City, April 9. Since accommodation at the Dolphin is limited, additional rooms have been reserved at the British Colonial Hotel. For reservations write directly to the Manager, Dolphin Hotel, Nassau, Bahamas (air mail requires a 10-cent stamp). The sixth Bahamas Medical Conference will be held Dec. 1-15. For information write Dr. B. L. Frank, Dolphin Hotel, Nassau, Bahamas.

General Practice Meeting in Dallas.—The 10th annual scientific assembly of the American Academy of General Practice will be held March 24-27 in the Memorial Auditorium, Dallas, Texas. The academy is presenting its assembly in combination with the Dallas Southern Clinical Society. Dr. Malcolm E. Phelps, El Reno, Okla., president of the academy, will open the meeting March 24. The program will feature 35 physician participants. Panel discussions will be held on "The Emotional and Physical Problems of Teenagers," "Diagnostic Clinic on X-ray Interpretation," "Electrocardiograms in Determining the Presence of Heart Disease," "Obstetrics," and "Urologic Problems in General Practice." Ninety scientific exhibits and 300 technical exhibits are planned. The president's reception and dance will be held March 28 at the Statler Hilton Hotel. A ladies' program is arranged, and a special luncheon entertainment is planned for the children. For information write the American Academy of General Practice, Volker Boulevard at Brookside, Kansas City 12, Mo.

Organize Allergy Photo Exhibit and Statistics Bureau.—The executive committee of the European Academy of Allergy has decided to organize—on the occasion of the meeting, "Occupational Allergy," to be presented for the European Academy of Allergy May 14-24 by the Netherlands Society of Allergy—a photo exhibition of (1) congress-photos of past allergy-congresses; (2) photos on allergic diseases (with a special group for occupational allergy); (3) photos on occupational medicine. For categories one and two a challenge-cup will be the first prize. Deadline for submission of photos is May 1.

A Bureau for Statistics will be established in Utrecht to coordinate for Europe the inquiry research work on allergic diseases, the statistics on frequency, mortability, etc. Anyone using inquiry-forms, to be filled up by some groups, or to be filled up by the examinators of some groups, is asked to send them. Send photos and statistical forms to and for information write Dr. W. J. Quarles van Ufford, Emmalaan 17, Utrecht, Netherlands.

Prize for Original Manuscripts.—Under the terms of the will of Dr. Martyn Paine (M.D., Harvard, 1816), the Robert Troup Paine Publication Fund has been established in memory of his son. A $3,000 prize will be awarded every four years to

the author or authors of a manuscript chosen to be the best work on a specified subject accepted by Harvard University Press during the preceding four years. The winning manuscript will be designated a prize treatise, and will be published by the university press. Authors will be paid royalties, as well as the prize. Eligible manuscripts must be original unpublished works of book length, and may be of single or multiple authorship. Any manuscript offered is eligible if its subject matter falls within the category and if it is accepted between the dates indicated:

I. The History of Religion (Jan. 1, 1958–Dec. 31, 1961).
II. The Principles of Commerce and Its Role in Society (Jan. 1, 1962–Dec. 31, 1965).
III. The History and/or Philosophy of Medicine (Jan. 1, 1966–Dec. 31, 1969).
IV. Law and Society (Jan. 1, 1970–Dec. 31, 1973).
V. The Principles of Inorganic Chemistry (Jan. 1, 1974–Dec. 31, 1977).
VI. Materia Medica and Therapeutics (Jan. 1, 1978–Dec. 31, 1981).

For information write Harvard University Press, 79 Garden St., Cambridge, Mass.

Society News.—Officers of the **American Academy of Allergy** are as follows: Dr. Max Samter, Chicago, president; Dr. Francis C. Lowell, Boston, president-elect; Dr. Jerome Glaser, Rochester, N. Y., vice-president; Dr. Bram Rose, Montreal, Canada, secretary; Dr. Isaac G. Blumstein, Philadelphia, treasurer; and Dr. Homer A. Howes, Detroit, historian (reelected to fifth term).—At the 11th annual meeting of the **American Electroencephalographic Society** the following officers were elected: president, Dr. Robert S. Dow, Portland, Ore.; president-elect, Dr. Wladimir T. Liberson, Rocky Hill, Conn.; secretary, Dr. Jerome K. Merlis, Baltimore; and treasurer, Peter E. Kellaway, Ph.D., Houston, Texas.—The **American Society of Clinical Pathologists** has installed the following officers: Dr. Harry P. Smith, New York City, president; Dr. Edward L. Burns, Toledo, Ohio, president-elect; and Dr. Joe M. Blumberg, Washington, D. C., vice-president.—Officers of the **Pacific Dermatologic Association** are as follows: president, Dr. Ervin H. Epstein, Oakland, Calif.; vice-president, Dr. Osgoode S. Philpott, Denver; secretary-treasurer, Dr. Louis H. Winer, Beverly Hills, Calif.; and assistant secretary, Capt. William N. New, M. C., U. S. N., San Diego, Calif.—The **American Association of Public Health Physicians** has installed the following officers: president, Dr. Sanford P. Lehman, Seattle; president-elect, Dr. John W. Cronin, Washington, D. C.; vice-president, Dr. Leroy L. Fatherree, Joliet, Ill.; secretary-treasurer, Dr. Joseph M. Bistowish, Tallahassee, Fla.; and executive secretary, Mr. William R. Harton, M.S.

a salute to
medical school progress
MEDICAL EDUCATION
WEEK ···· April 20-26

LATIN AMERICA

Psychology Meeting in Rio de Janeiro.—The third Ibero-American Medical Psychological Meeting will be held Aug. 17-23 in Rio de Janeiro, Brazil. The themes are: (1) Hormones, Instincts, Neural Integration; (2) Digestive Psychosomatic Pathology; and (3) The Doctor-Patient Relationship (the understanding of transference for the medical formation). There will not be free presentation of works by the participants. Themes were given to a certain number of speakers. After the presentation of their reports, they will meet, in a round-table discussion, to answer questions. Coordinators for the meeting are professors Decio Soares de Souza, Thales Martins, Clementino Fraga Filho, and Dr. Walderedo Ismael de Oliveira, from the University of Brazil. For information write the Instituto de Psiquiatria da Universidade do Brazil, Av. Wenceslau Braz, 71- Botafogo, Rio de Janeiro, Brazil.

CORRECTION

Longevity of Physicians.—In the article by Raymond Seltser and Philip E. Sartwell, entitled Ionizing Radiation and Longevity of Physicians, in the Feb. 8, 1958, issue of THE JOURNAL, page 586, figures 1 and 2 were transposed in relation to the legends.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. *First Examination.* Medical Schools in the United States, March 25. Final date for filing application was Feb. 10. *Second Examination.* Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 17-19. Sec., Dr. D. G. Gill, State Office Building, Montgomery 4.

ARIZONA:* *Examination and Reciprocity.* Phoenix, April 16-18. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

CALIFORNIA: *Written. Examination.* San Francisco, June 16-19; Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, June 14; Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

COLORADO:* *Examination and Reciprocity.* Denver, June 10-11. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

DELAWARE: *Examination and Reciprocity.* Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

FLORIDA:* *Examination.* Miami, June 29-July 1. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami.

GEORGIA: *Examination and Reciprocity.* Atlanta and Augusta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta.

IDAHO: *Examination.* Boise, July 14-16. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination and Reciprocity.* Chicago, April 7-10. Superintendent of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 18-20. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

LOUISIANA: *Examination and Reciprocity.* New Orleans, June 5-7. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans.

MARYLAND: *Examination.* Baltimore, June 17-20. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 15-18. Sec., Dr. Robert C. Cochrane, Room 37 State House, Boston.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 9-11. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MICHIGAN:* *Examination.* Minneapolis, April 15-17. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: *Examination and Reciprocity.* Helena, April 1. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June. Sec., Mr. Husted K. Watson, Room 1069, State Capitol Bldg., Lincoln 9.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, May 19-20. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, New York City and Syracuse, June 24-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Endorsement.* Asheville, May 5. *Examination.* Raleigh, June 16-19. *Endorsement.* Raleigh, June 17. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Endorsement.* Columbus, April 1; *Examination.* June 19-21. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 3-4. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, April 11-12. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July 8-10. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Endorsement.* Providence, March 20. *Examination.* Providence, April 3-4. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TENNESSEE:* *Examination.* Memphis, March 19-20. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 23-25. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, July 9-11. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Address: Board of Medical Examiners, 631 First St., S.W., Roanoke.

WASHINGTON:* *Examination.* Seattle, July 14-16. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WEST VIRGINIA: *Examination and Reciprocity.* Charleston, April 14 and July (date not set). Sec., Dr. N. H. Dyer, State Office Bldg., No. 5, Charleston.

WISCONSIN:* *Endorsement.* Madison, April 25. *Examination.* Milwaukee, July 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 2. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

ARIZONA: *Examination.* Tucson, March 18. Sec., Mr. Herman C. Bateman, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, May 5-6. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

COLORADO: *Examination and Endorsement.* Denver, May 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

CONNECTICUT: *Examination and Endorsement.* New Haven, June 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 14-15. Deputy Director, Commission on Licensure, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

FLORIDA: *Examination.* Miami, June 7. Sec., Mr. M. W. Emmel, Box 340, Gainesville.

IOWA: *Examination.* Des Moines, April 8. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

KANSAS: *Examination.* Kansas City, June 3-4. Sec., Dr. R. E. Stowell, University of Kansas School of Medicine, Kansas City 12.

MINNESOTA: *Examination.* Minneapolis, April 1-2. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.

NEW MEXICO: *Examination.* Santa Fe, April 20. *Reciprocity.* Santa Fe, March 26. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, April 4-5. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

SOUTH DAKOTA: *Examination.* Vermillion, June 6-7. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

RHODE ISLAND: *Endorsement.* Providence, April 30. *Examination.* Providence, May 14. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TENNESSEE: *Examination.* March 19-20, Memphis and Nashville. Sec., Dr. O. W. Hyman, 62 S. Dunlap St., Memphis.

TEXAS: *Examination.* April 18-19, Austin, Galveston and Houston. Sec., Bro. Raphael Wilson, 407 Perry Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, March 29, Milwaukee, June 7. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

*Basic Science Certificate required.

GOVERNMENT SERVICES

PUBLIC HEALTH SERVICE

Research Grants and Fellowships.—The National Institutes of Health of the Public Health Service awarded 215 research grants totaling $3,240,440 during the month of January. Research fellowships totaling $2,639,579 were awarded during the period from July, 1957, through January, 1958, the service has announced.

The research grants were made to 115 institutions in 32 states, the District of Columbia, 2 territories, and 5 foreign countries. The major portion of these grants provides support in the fields of cardiac and cancer research. Seventy grants, totaling $745,955, have been awarded for new projects. The remaining grants represent continuations of or supplements to existing projects. The research fellowships were awarded to 583 individuals in 169 institutions. These are located in 39 states, the District of Columbia, one territory, and 7 foreign countries.

Research grants support research projects in health, medicine, and allied fields. They are intended to expand medical and biological research activities in universities and other institutions throughout the country. Research fellowships support research training of (1) students in medical, dental, nursing, and public health schools; (2) candidates for master's and doctorate degrees in the biological sciences; and (3) research scientists at various levels of training following receipt of the doctorate.

Advisory Committee on Radiation.—The surgeon general has announced the establishment of a National Advisory Committee on Radiation to advise his office on the further development of service programs dealing with public health aspects of radiation from all sources. Last August, the surgeon general appointed Dr. Russell H. Morgan, professor of radiology, Johns Hopkins University Medical School, as special consultant on the public health aspects of radiation. Dr. Morgan will serve as chairman of the new committee, which will hold its initial meeting March 13; others appointed to the committee so far are as follows: Arnold O. Beckman, president, Beckman Instruments, Inc., Fullerton, Calif.; Victor P. Bond, pathology division, Brookhaven National Laboratory, Upton, Long Island, New York; Richard H. Chamberlain, professor of radiology, Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia 4; James F. Crow, professor of genetics, University of Wisconsin, Madison 6, Wis.; Herman E. Hilleboe, state commissioner of health, 84 Holland Ave., Albany, N. Y.; Edward B. Lewis, professor of biology, California Institute of Technology, Pasadena, Calif.; Berwyn F. Mattison, executive secretary, American Public Health Association, 1790 Broadway, New York 27; Lauriston S. Taylor, chief, atomic radiation physics division, National Bureau of Standards, Washington 25, D. C.; George W. Thorn, physician-in-chief, Peter Bent Brigham Hospital, Boston 15; Abel Wolman, professor of sanitary engineering, Johns Hopkins University, Baltimore.

Regular Corps Examinations for Medical Officers.—A competitive examination for appointment of medical officers to the Regular Corps of the U. S. Public Health Service will be held in various places throughout the country on May 6 to 9, 1958. Appointments provide opportunities for career service in clinical medicine, research, and public health. Entrance pay for assistant and senior assistant surgeons with dependents is $7,498 (assistant grade applicants are assigned the temporary grade of senior assistant). Provisions are made for promotions at regular intervals. Benefits include periodic pay increases, 30 days annual leave, sick leave, medical care, disability retirement pay, retirement pay which is three-fourths of annual basic pay at time of retirement, and other privileges.

Active duty as a Public Health Service officer fulfills the obligation of Selective Service. Requirements for both ranks are U. S. citizenship, age of at least 21 years, and graduation from a recognized school of medicine. For the rank of assistant surgeon, at least seven years of collegiate and professional training and appropriate experience are needed. For senior assistant surgeon, an additional 3 years, for a total of at least 10 years of collegiate and professional training and appropriate experience, are needed. Entrance examinations will include an oral interview, physical examination, and comprehensive objective examinations in the professional field.

Application forms may be obtained from the Surgeon General, Public Health Service (P), Washington 25, D. C. Completed application forms must be received in the Division of Personnel no later than April 11, 1958.

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DEATHS

Abbot, Edward Stanley ● Wayland, Mass.; Harvard Medical School, Boston, 1893; member of the American Psychiatric Association and the American Psychopathological Association; past-president of the Boston Society of Psychiatry and Neurology; at one time on the faculty of his alma mater; veteran of World War I; formerly associated with the McLean Hospital in Waverly and assistant superintendent of the Boston City Hospital; died in Weston Oct. 15, aged 93.

Alden, Maurice ●New York City; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1906; associated with Lutheran Hospital; died in Berlin, Germany, Oct. 21, aged 75, of carcinoma of the lung.

Applegate, Matthew Mullin, Cincinnati; Medical College of Ohio, Cincinnati, 1909; died in the Veterans Administration Hospital, Lexington, Ky., Nov. 15, aged 73.

Arendt, Erich J. ● San Antonio, Texas; American Medical College, St. Louis, 1904; for many years city health officer; associated with the Nix Hospital; died Dec. 24, aged 78, of a heart attack.

Arnow, Matthew, Eustis, Fla.; Rush Medical College, Chicago, 1937; associated with Waterman Memorial Hospital, where he died Dec. 29, aged 45, of viral pneumonitis.

Baum, Felix ● South Orange, N. J.; born Feb. 20, 1883; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1908; member of the American College of Chest Physicians and the American Trudeau Society; at one time assistant professor of medicine at the University of Colorado School of Medicine in Denver, where he was medical director of the National Jewish Hospital; served on the staffs of the Deborah Tuberculosis Sanatorium in Browns Mill, Essex County Sanitarium, Verona, and St. Mary's Hospital in Orange; died Jan. 7, aged 74, of coronary thrombosis.

Beardsley, Wayne Roscoe, Major, U. S. Army, retired, Jones, Mich.; Jefferson Medical College of Philadelphia, 1910; commissioned in the medical corps of the U. S. Army in 1917 and retired in November, 1930; medical director of the Cass County Hospital in Cassopolis; died in the Lakeview Hospital, Paw Paw, Dec. 9, aged 73, of arteriosclerotic cardiovascular disease.

● Indicates Member of the American Medical Association.

Beasley, John Snodgrass, Centerville, Tenn.; University of Tennessee Medical Department, Nashville, 1901; served as mayor and for many years county health officer; died Dec. 25, aged 77.

Bell, Robert H. ● Carlinville, Ill.; Washington University School of Medicine, St. Louis, 1906; formerly associated with the Illinois Department of Public Health; served on the staff of the Carlinville Area Hospital; died Dec. 25, aged 76, of cirrhosis of the liver.

Blum, Charles N., Syracuse, N. Y.; Syracuse University College of Medicine, 1897; died Dec. 22, aged 81, of skin cancer.

Borreson, Baldwin, Bemidji, Minn.; University of Minnesota Medical School, Minneapolis, 1915; served as superintendent of the Oakland Park Sanatorium in Thief River Falls, and medical director and superintendent of the Sunnyrest Sanatorium in Crookston; died in the Veterans Administration Hospital, Fargo, N. D., Nov. 6, aged 71, of cerebral thrombosis.

Bradley, Raymond Leslie, Houston, Texas; University of Texas School of Medicine, Galveston, 1918; formerly on the faculty of the Baylor University College of Medicine; member of the staffs of St. Joseph's and Methodist hospitals; died Dec. 24, aged 65.

Broughton, Nathaniel Joseph, Lorain, Ohio; Meharry Medical College, Nashville, 1905; died Dec. 28, aged 79, of nephrosclerosis and uremia.

Broyles, Samuel Kenneth ● Amarillo, Texas; University of Tennessee College of Medicine, Memphis, 1925; veteran of World War I; associated with St. Anthony's Hospital; died Dec. 23, aged 59.

Bruck, Samuel, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1907; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; an associate member of the American Medical Association; associated with the Northeastern Hospital, where he was medical director for four years and where he died Jan. 10, aged 72.

Buchan, Edward James, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; formerly member of the state boxing commission; served on the staff of the Augustana Hospital; died Jan. 20, aged 77, of a heart attack.

Bullock, William Battle, Oxford, N. C.; Bellevue Hospital Medical College, New York City, 1892; died in Crewe, Va., Jan. 2, aged 88.

Burke, William Adam ● Pottsville, Pa.; Jefferson Medical College of Philadelphia, 1918; member of the American Academy of General Practice; associated with Pottsville Hospital; died in Jefferson Medical College Hospital, Philadelphia, Jan. 6, aged 63, of injuries received in an automobile accident.

Burrows, Gene, Chicago; Chicago Medical School, 1917; died in St. Francis Hospital, Blue Island, Jan. 8, aged 76, of multiple myeloma.

Calkum, John Foley, Alamogordo, N. Mex.; University of Colorado School of Medicine, Denver, 1955; interned at St. Joseph's Hospital in Denver; service member of the American Medical Association; captain in the medical corps of the U. S. Air Force Reserve, serving in the School of Aviation Medicine at Gunter Air Force Base in Montgomery, Ala.; died near Benton, Ala., Dec. 19, aged 29, in a civilian aircraft accident.

Campbell, John Ross ● Pratt, Kan.; University of Kansas School of Medicine, Kansas City, Kan., 1915; veteran of World War I; on the staff of the Pratt County Hospital, where he died Dec. 19, aged 68, of uremia.

Carr, Bella, Duarte, Calif.; Université de Paris Faculté de Médecine, France, 1900; for many years associated with the City of Hope; died Dec. 24, aged 81.

Carter, Clifford Charles ● Flushing, N. Y.; St. Louis University School of Medicine, 1938; certified by the National Board of Medical Examiners; veteran of World War II; died in the Kew Gardens (N. Y.) General Hospital Jan. 12, aged 42.

Colwick, James Thomas ● Durant, Okla.; born Feb. 24, 1888; Southern Methodist University Medical Department, Dallas, Texas, 1912; member of the American Academy of General Practice; past-president of the Atoka–Bryan–Coal Counties Medical Society; for many years member of the city council; veteran of World War I; served as medical adviser to the Bryan County Selective Service Board and was awarded a merit of honor by the Oklahoma Selective Service Board for his outstanding service during World War II; associated with the Durant Hospital; died Dec. 15, aged 69, of pulmonary embolism and myocardial insufficiency.

Conrad, Adolph Henry ● St. Louis; born in 1884; St. Louis University School of Medicine, 1906; associate clinical professor emeritus of dermatology at Washington University School of Medicine; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; formerly vice-president of the Southern Medical Association; associated with St. Louis County Hospital in Clayton, Barnard Free Skin and Cancer Hospital, Barnes Hospital, Hospital of the Masonic Home, Jewish Hospital, Shriners' Hospital for Crippled Children, and St. Louis Maternity Hospital; died Jan. 1, aged 73.

Cox, Hugh Michael, New York City; Albany (N. Y.) Medical College, 1902; an associate member of the American Medical Association; associated with Long Beach Memorial Hospital in Long Beach, N. Y., and Manhattan State Hospital and St. Clare's Hospital; president emeritus of Misericordia Hospital, where for many years he was director of medicine; died in the Veterans Administration Hospital Jan. 6, aged 80.

Cox, James Francis ● Chicago; Rush Medical College, Chicago, 1909; retired medical director of the Illinois Bell Telephone Company; died in the Garfield Park Community Hospital Jan. 9, aged 74.

Curtis, Austin Maurice Jr., Paterson, N. J.; Howard University College of Medicine, Washington, D. C., 1914; member of the Medical Society of New Jersey; on the courtesy staffs of the Paterson General Hospital and the Barnert Memorial Hospital, where he died Jan. 2, aged 66, of arteriosclerotic heart disease.

Dearing, Bradford French ● San Francisco; Washington University School of Medicine, St. Louis, 1917; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; formerly assistant clinical professor of pediatrics at the University of California School of Medicine; served overseas during World War I; associated with French Hospital and University of California hospitals; died Jan. 5, aged 67, of a heart attack.

Dessent, Robert ● Chicago; University of Illinois College of Medicine, Chicago, 1924; clinical assistant professor of pediatrics at his alma mater; since 1943 epidemiologist and director of maternal and child hygiene for the Cook County Health Department; field health officer for the board of health of Chicago from 1927 to 1941; served as district health superintendent of Illinois for the department of public health; veteran of World War I; died in the Michael Reese Hospital Jan. 14, aged 58, of acute myocardial infarction and arteriosclerotic heart disease.

Donald, William Goodricke ● Berkeley, Calif.; born in San Francisco Nov. 2, 1889; University of California School of Medicine, San Francisco, 1923; member of the Industrial Medical Association, American Association for the Advancement of Science, World Medical Association, and the California Academy of Medicine; past-president of the

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Alameda County Medical Society; served in the sanitary corps of the Army during World War I; university physician, University of California; associated with the Alta Bates, Herrick Memorial, and Peralta hospitals; died Dec. 30, aged 68, of acute myocardial infarction.

Dotye, Christopher Benjamin, Danville, Ky.; Meharry Medical College, Nashville, Tenn., 1930; died in the Ephraim McDowell Memorial Hospital Dec. 15, aged 55, of cerebral thrombosis.

Eiel, Merrill Orion • Osage, Iowa; State University of Iowa College of Medicine, Iowa City, 1927; member of the staff, Mitchell County Memorial Hospital; died Dec. 15, aged 54, of coronary occlusion.

Erickson, John Lynn, Fergus Falls, Minn.; University of Minnesota Medical School, Minneapolis, 1923; associated with Fergus Falls State Hospital; died Dec. 26, aged 69, of coronary thrombosis.

Farley, Robert Howard, North Hill, Pa.; Hering Medical College, Chicago, 1911; veteran of World War I; an associate member of the American Medical Association; served on the staffs of Hahnemann and Germantown hospitals; died Jan. 16, aged 71, of coronary infarction and arteriosclerotic heart disease.

Fennel, Eric Adolphus • Honolulu, Hawaii; University of Cincinnati College of Medicine, 1912; member of the College of American Pathologists; died in the Queen's Hospital Dec. 24, aged 70, of coronary thrombosis.

Field, Francis Floyd, Marion, Ohio; Starling Medical College, Columbus, 1898; veteran of World War I; died Dec. 11, aged 81, of a heart attack.

Finnegan, Philip Joseph • Salem, Mass.; Harvard Medical School, Boston, 1911; retired Salem health board physician; veteran of World War I; examining physician for the Selective Service Board during World War II; served on the staffs of the Josiah B. Thomas Hospital in Peabody and the Salem Hospital, where he died Dec. 18, aged 70, of dissecting aneurysm.

Forster, Neslen Kelliher • Pacific Palisades, Calif.; born in Missoula, Mont., Dec. 30, 1892; University of Illinois College of Medicine, Chicago, 1919; certified by the National Board of Medical Examiners; member of the Central Association of Obstetricians and Gynecologists, American Urological Association, American Academy of Dermatology and Syphilology, and the Industrial Medical Association; fellow of the International College of Surgeons and the American College of Surgeons; formerly practiced in Hammond, Ind., where he was on the staff of St. Margaret's Hospital, and was past-president of the Lake County Medical Society; associated with St. John's Hospital in Santa Monica and the Culver City Hospital and the Community Hospital in Culver City; died Dec. 31, aged 65.

Fortun, Olav Johan • Seattle; Chicago College of Medicine and Surgery, 1910; died Dec. 8, aged 83, of coronary thrombosis.

Francez, Zachary J., Crowley, La.; University of Tennessee Medical Department, Nashville, 1903; for many years parish coroner; died in the Acadia Hospital Dec. 9, aged 76, of pneumonia.

Franklin, William David, Walnut Grove, Miss.; Mississippi Medical College, Meridian, 1907; died Oct. 29, aged 89, of uremia and chronic nephritis.

Frechtling, Louis Henry, Hamilton, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; for many years associated with the Medical Department of Champion Paper and Fibre Company; examining physician during World War I for the Butler County Draft Board served on the board of education; for many years on the board of directors of the Home Federal Savings and Loan Association of Hamilton; died Dec. 10, aged 77, of adenocarcinoma of the pylorus.

Friedman, Henry • Granville, N. Y.; University of Edinburgh Faculty of Medicine, Scotland, 1935; associated with the Emma Laing Stevens Hospital in Granville and the Glens Falls (N. Y.) Hospital; died Dec. 11, aged 49, of coronary occlusion.

Gaev, Samuel David • Philadelphia; Temple University School of Medicine, Philadelphia, 1934; served overseas during World War II; associated with Philadelphia General, Temple University, and Episcopal hospitals; died in Atlantic City (N. J.) Hospital Jan. 6, aged 49, of acute coronary occlusion.

Gage, Idys Mims • New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1917; professor of clinical surgery at his alma mater; member of the founders group of the American Board of Surgery; chairman of the Section on Surgery, General and Abdominal, 1951-1952, American Medical Association; member and past-president of the Southern Surgical Association and New Orleans Surgical Society; in 1949 secretary of the 13th Congress of the International Surgical Society in Brussels, Belgium; member of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; veteran of World War I; served during World War II and was awarded the Legion of Merit in 1946 for exceptional service as consultant in surgery to the Fourth Service Command of Army; associated with Ochsner Clinic and the Ochsner Foundation Hospital; served on the staffs of the Illinois Central Hospital, Touro In-

firmary, and the Charity Hospital of Louisiana; died in the Methodist Hospital, Houston, Dec. 19, aged 64.

Gardiner, Mildred White ● Middletown, Ohio; Ohio State University College of Medicine, Columbus, 1925; member of the American Society of Anesthesiologists; associated with the Middletown Hospital; died in Cincinnati Dec. 21, aged 65, of coronary occlusion.

Giuseffi, Jerome Jr., Cincinnati; University of Cincinnati College of Medicine, 1942; assistant professor of surgery at his alma mater; specialist certified by the American Board of Surgery; veteran of World War II; associated with Our Lady of Mercy Hospital, Bethesda Hospital, and the Christian R. Holmes Hospital, where he died Jan. 2, aged 39.

Greaves, Blanche F., Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1895; served on the staffs of the Hospital of the Woman's Medical College and the Doctors Hospital, where she died Jan. 13, aged 89, of congestive heart failure.

Gilman, Ernest L., Mellen, Wis.; Milwaukee Medical College, 1911; served as city health officer; associated with St. Joseph's Hospital in Ashland; died Dec. 10, aged 73, of coronary thrombosis.

Graves, Harriett M. Daniel ● Murphysboro, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1906; formerly associated with the state health department; served as secretary of the Jackson County Medical Society; on the staff of St. Andrew's Hospital; died Nov. 26, aged 86.

Gregg, Alfred Dickson, Henderson, N. C.; Medical College of South Carolina, Charleston, 1913; veteran of World War I; county health officer; died in the Maria Parham Hospital Dec. 17, aged 74, of arteriosclerotic heart disease.

Griffin, Edwin Albert ● Brooklyn; born in New York City May 25, 1887; University and Bellevue Hospital Medical College, New York City, 1909; specialist certified by the American Board of Otolaryngology; past-president of the Pan American Medical Association; served as vice-president of the Kings County Medical Society; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, American Oto-rhinologic Society for Plastic Surgery, and American College of Allergists; fellow of the American College of Surgeons and the International College of Surgeons; served on the faculty of the Long Island College of Medicine; associated with Brooklyn Eye and Ear, Samaritan, and Methodist hospitals; died Dec. 29, aged 70, of cardiac failure.

Hall, Rufus Warren ● Trumbull, Conn.; Yale University School of Medicine, New Haven, 1907; died Dec. 19, aged 79.

Harrington, Fred Blanchard ● Steubenville, Ohio; University of Buffalo School of Medicine, 1914; member of the Industrial Medical Association; for many years secretary of the Hancock County Medical Society; veteran of World War I; chief surgeon of the Weirton Steel Company from 1919 to 1936 when he became part-time surgeon; president of the staff, Ohio Valley Hospital; member of the staffs of Weirton (Ohio) General Hospital and the Gill Memorial Hospital; died Dec. 24, aged 69, of coronary occlusion.

Hartman, George W., San Francisco; Johns Hopkins University School of Medicine, Baltimore, 1908; assistant clinical professor of surgery at Stanford University School of Medicine; specialist certified by the American Board of Urology; an associate member of the American Medical Association; member of the American Urological Association, and past-president and secretary of the Western Branch; associated with Mount Zion and Polyclinic hospitals and the Stanford University Hospital, where he died Dec. 24, aged 78.

Head, Homer ● Monroe, Ga.; University of Georgia School of Medicine, Augusta, 1939; served as president of the Walton County Medical Society; county physician; on the staff of the Walton County Hospital; died in St. Mary's Hospital, Athens, Dec. 17, aged 44, of hepatitis.

Henderson, Harry Allen, Wheeling, W. Va.; Western Pennsylvania Medical College, Pittsburgh, 1896; served as medical director of the Ohio County public schools; formerly member of the staffs of Ohio Valley General Hospital and Wheeling Hospital, where he died Dec. 13, aged 87, of paralytic ileus and intestinal obstruction.

Hendry, Hugh William, Detroit; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1920; member of the Michigan State Medical Society; served with the Canadian Expeditionary Force in France during World War I; died in the Pontiac (Mich.) General Hospital Nov. 26, aged 64, of congestive heart failure.

Hunt, Sheldon Leslie, Yarmouth Port, Mass.; Tufts College Medical School, Boston, 1936; member of the Massachusetts Medical Society; veteran of World War II; on the staff of the Cape Cod Hospital in Hyannis; died Dec. 21, aged 46.

Ingram, Glen Ray ● Champaign, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1916; associated with the Mercy Hospital in Urbana, and the Burnham City Hospital, where he died Dec. 10, aged 70, of coronary thrombosis.

Miller, J. Preston, Miami, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1896; died Dec. 21, aged 88.

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Paton, Fred Wade, Bradford, Pa.; Columbia University College of Physicians and Surgeons, New York City, 1909; an associate member of the American Medical Association; on the staff of the Bradford Hospital, where he died Dec. 22, aged 75, of cerebral hemorrhage.

Patton, Oliver Beirne, Huntsville, Ala.; University of Virginia Department of Medicine, Charlottesville, 1905; died in the Huntsville Hospital Dec. 25, aged 82, of arteriosclerosis.

Roane, John Quincy ✱ Carlyle, Ill.; Missouri Medical College, St. Louis, 1898; for many years secretary of the Clinton County Medical Society, of which he was past-president; a vice-president and director of First National Bank of Carlyle; associated with St. Joseph's Hospital in Breese, where he died Dec. 29, aged 83, of chronic myocarditis.

Rogers, Weaver Burnside, Clarksburg, W. Va.; Baltimore Medical College, 1907; veteran of World War I; served as superintendent of the Huntington (W. Va.) State Hospital and the Barboursville (W. Va.) State Hospital; formerly associated with Spencer (W. Va.) State Hospital; died Dec. 31, aged 77, of asthma and cardiac dilatation.

Rosenbaum, Jack Davidson, Boston; born in New Haven, Conn., Sept. 12, 1912; Yale University School of Medicine, New Haven, Conn., 1937; specialist certified by the American Board of Internal Medicine; certified by the National Board of Medical Examiners; member of the American Society of Clinical Investigation, American Federation for Clinical Research, American Diabetes Association, American Association for the Advancement of Science, Phi Beta Kappa, Sigma Xi, and Alpha Omega Alpha; fellow of the American College of Physicians; service member of the American Medical Association; clinical professor of medicine at Tufts College Medical School; served on the faculty of his alma mater and the Boston University School of Medicine; veteran of World War II; assistant chief in medicine at the Veterans Administration Hospital; served as assistant chief of the medical service and director of the research laboratory, Cushing Veterans Hospital in Framingham, and as associate physician at the New Haven (Conn.) Hospital; died Dec. 16, aged 45, of cancer of the transverse colon.

Roswell, Joseph T. ✱ Woonsocket, R. I.; Bellevue Hospital Medical College, New York City, 1894; honorary member of the staff of the Woonsocket Hospital; died Dec. 20, aged 91, of myocardial insufficiency.

Rugeley, Frank Robert ✱ Wharton, Texas; University of Texas School of Medicine, Galveston, 1933; member of the American College of Allergists and the American Academy of General Practice; one of the founders of the Rugeley-Blasingame Clinic-Hospital; died Dec. 21, aged 49.

Ruskin, Simon Lyon ✱ New York City; University and Bellevue Hospital Medical College, New York City, 1920; member of the American Chemical Society; specialist certified by the American Board of Otolaryngology; associated with the Bronx Hospital; director of the Ruskin Research Foundation; died Jan. 1, aged 60.

Ryle, John Francis, New York City; Yale University School of Medicine, New Haven, Conn., 1902; an associate member of the American Medical Association; on the staff of the Misericordia Hospital, where he died Jan. 1, aged 79, of benign prostatic hypertrophy and hemorrhage following prostatectomy.

Sabshin, Zalman Isaac, Miami Beach, Fla.; Long Island College Hospital, Brooklyn, 1917; an associate member of the American Medical Association; member of the Medical Society of the State of New York; formerly practiced in New York City, where he was on the staff of the Bronx Hospital; died in Mount Sinai Hospital Dec. 21, aged 65, of cerebral hemorrhage.

Schwarz, Frank William ✱ Battle Creek, Mich.; Temple University School of Medicine, Philadelphia, 1917; member of the American Psychiatric Association; veteran of World War I; served with the Veterans Administration; associated with the Community and Leila Y. Post Montgomery hospitals; died Dec. 27, aged 70, of arteriosclerosis.

Shafer, Clare Field, Grafton, W. Va.; Medical College of Virginia, Richmond, 1909; an associate member of the American Medical Association; served as county health officer; on the staff of the Grafton City Hospital, where he died Dec. 28, aged 75, of bilateral bronchopneumonia.

Shipp, Henry Harris, Woodsboro, Texas; Atlanta College of Physicians and Surgeons, 1902; veteran of the Spanish–American War; died Dec. 22, aged 78.

Sims, Paul Martin Jr. ✱ Beaumont, Texas; University of Texas School of Medicine, Galveston, 1947; veteran of the Korean War; died Dec. 27, aged 33.

Smith, Myrtle ✱ Worcester, Mass.; Tufts College Medical School, Boston, 1905; for many years practiced in Shrewsbury, where she was a trustee of the public library; served on the staff of the Memorial Hospital; associated with Fallon Clinic; died Dec. 13, aged 78, of acute pulmonary edema.

Smyth, Margaret Hamilton, Saratoga, Calif.; Cooper Medical College, San Francisco, 1898; member of the American Psychiatric Association; past-president of the San Joaquin County Medical Society; served as medical director and superintendent of the Stockton (Calif.) State Hospital; died in Palo Alto Dec. 30, aged 82, of bronchopneumonia.

Soifer, Samuel ● New York City; Long Island College Hospital, Brooklyn, 1911; died Nov. 20, aged 74, of heart failure.

Speidel, Roy Edward, Senath, Mo.; St. Louis University School of Medicine, 1924; died Dec. 25, aged 63.

Sprafka, Joseph Michael ● St. Paul; University of Minnesota Medical School, Minneapolis, 1920; associated with St. John's, Miller, and St. Luke's hospitals and St. Joseph's Hospital, where he died Dec. 6, aged 63, of cancer.

Stanton, Frank W. ● Joliet, Ill.; Illinois Medical College, Chicago, 1907; died Dec. 10, aged 77.

Steinberg, Meyer Jerome ● Chicago; Rush Medical College, Chicago, 1926; specialist certified by the American Board of Internal Medicine; clinical associate professor of medicine at the Chicago Medical School; veteran of World War II; associated with Cook County and the Louis A. Weiss Memorial hospitals, and the Highland Park (Ill.) Hospital, where he died Jan. 6, aged 54, of heart disease.

Stewart, Horace Gentry ● Cincinnati; Johns Hopkins University School of Medicine, Baltimore, 1918; died Dec. 24, aged 68.

Stolz, Bernard, Troy, N. Y.; Rheinische Friedrich–Wilhelms–Universität Medizinische Fakultät, Bonn, Prussia, Germany, 1924; member of the Medical Society of the State of New York; died in St. Mary's Hospital Dec. 26, aged 57.

Stotz, Kenneth Frederick ● Chicago; born in Chicago Aug. 16, 1909; Northwestern University Medical School, Chicago, 1934; member of the Industrial Medical Association; served as president and vice-president of the Chicago Society of Industrial Medicine and Surgery; veteran of World War II and was presented with the Legion of Merit award "for exceptionally meritorious conduct in the performance of outstanding services to the South Pacific Area from March, 1942, to May, 1944"; on the staffs of the Walther Memorial and Norwegian American hospitals; died Jan. 3, aged 48, of acute coronary heart disease, cholelithiasis, and acute cholecystitis.

Thomason, Henry Eagle ● Summers, Ark.; Beaumont Hospital Medical College, St. Louis, 1900; St. Louis University School of Medicine, 1902; member of the Missouri State Medical Association and the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; for many years practiced in Kansas City, Mo., where he was associated with St. Mary's Hospital; died in McAllen, Texas, Dec. 10, aged 80, of cerebral hemorrhage.

Valente, Frank A. ● Buffalo; University of Buffalo School of Medicine, 1908; associated with the Sisters of Charity Hospital; died Dec. 17, aged 74, of carcinoma of the pancreas.

Weaver, Davis Charles, New York City; Columbia University College of Physicians and Surgeons, New York City, 1948; interned at the Bellevue Hospital; served a residency at the Homer Folks Tuberculosis Hospital in Oneonta, N. Y., and St. Luke's Hospital; died Dec. 20, aged 32.

Weiss–Robertson, Frieda Emma, Cleveland; Cleveland Homeopathic Medical College, 1903; served on the staffs of the Woman's and Huron Road hospitals; died Dec. 23, aged 80.

Wenger, Oliver Clarence, Medical Director, U. S. Public Health Service, retired, Hot Springs National Park, Ark.; born in St. Louis Sept. 2, 1884; St. Louis University School of Medicine, 1908; served as diagnostician with the St. Louis Health Department; his military services included a tour of duty with the Philippine Islands Constabulary during the years 1912 to 1915; a captain in the sanitary corps of the American Expeditionary Forces during World War I; during World War II served on the staff of the Caribbean Defense Command, wherein, as liaison officer, developed health programs involving local populations and the armed forces; these programs were carried out under the auspices of the Anglo-American Caribbean Commission; for these latter services was decorated by King George VI of England with the Order of the British Empire; specialist certified by the American Board of Preventive Medicine; joined the staff of the U. S. Public Health Service in 1919 and retired in 1945; chief epidemiologist on the staff of the Chicago Board of Health; fellow of the American College of Physicians; associated with the Leo N. Levi Memorial Hospital; died in the U. S. Public Health Service Hospital in Chicago Jan. 6, aged 73, of acute myocardial infarction and arteriosclerosis.

Weston, Ursa Cleveland ● Galt, Mo.; University Medical College of Kansas City, 1910; veteran of World War I; died in the Cullers Hospital in Trenton, Dec. 24, aged 72.

Young, Charles Stephen ● Los Angeles; College of Physicians and Surgeons, medical department of the University of Southern California, Los Angeles, 1914; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; veteran of World War I; associated with California Hospital, Methodist Hospital of Southern California, Orthopaedic Hospital, and Presbyterian Hospital–Olmsted Memorial; died in the Good Samaritan Hospital Dec. 15, aged 65.

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FOREIGN LETTERS

AUSTRIA

Malacia, Pseudomalacia, and Osteoporosis.—The annual meeting of Austrian physicians in September was arranged by the Van-Swieten Society in Vienna to coincide with the meetings of several of the societies of medical specialties. Dr. L. Haslhofer of Vienna stated that although histological differentiation and a definite diagnosis is not possible in every case in the diagnosis of skeletal diseases, biopsy should be used more widely. Dr. G. Fanconi of Zurich said that primary hypophosphatasia, in which vitamin D acts as a toxin, and osteogenesis imperfecta are congenital porotic disorders. Acquired porotic diseases include particularly that due to inactivity in which, as the result of immobilization, Sudeck's atrophy and in many cases a secondary hyperparathyroidism may develop. This condition may be differentiated from primary hyperparathyroidism by the roentgenologic demonstration of the "lamina dura" around the roots of the permanent teeth. In secondary hyperparathyroidism, which may develop in any condition in which the calcium content of the blood is lowered and the phosphate content is increased, it is sometimes possible to demonstrate an acro-osteolysis. In Cushing's disease, endocrinogenic porosis may develop as the result of the inhibition of the osteoblasts by an increase in cortisone. The bone lesions secondary to renal disease generally show the character of a malacia and develop either as the result of glomerular insufficiency or of a phosphate diabetes caused by tubular dysfunction.

Dr. H. Ellegast pointed out that porosis and malacia are readily differentiable in the roentgenogram. Porotic conditions are characterized by sharp contours, clear, fine-to-coarse strands in the structure, and general increase in permeability to roentgen rays. Malacia, on the other hand, is characterized by indistinct contours, washed-out, indistinct structures, and by typical localization.

Dr. H. Jesserer of Vienna stated that the clinical aspects are particularly important for the early diagnosis of skeletal diseases, because the roentgenological signs do not appear until the process is advanced. Since the symptoms are rarely pathognomonic, laboratory tests must be resorted to for corroboration. The blood phosphate level is more significant than that of calcium. The alkaline phosphatase level is a standard of measurement for osteoblastic activity, and the Sulkowitch test is a measure of the calciuria. In osteogenesis imperfecta, fractures are as a rule a threat only up to the age of 18. After that, until the age of presenile porosis, fractures are rare. Thus, there is a possibility of a combination of this congenital porosis with malacic diseases. The theory that the development of presenile porosis is the result of the cessation of the function of the gonads seems to be disproved by the fact that even in women who have been castrated because of a carcinoma at a relatively early age, it did not develop until the age at which it developed in noncastrated women. The fact that hormone therapy is without effect if it is not combined with physical exercise also supports this revised viewpoint. In order to avoid complications, the therapeutic use of vitamin D in patients with malacia should always be preceded by a Sulkowitch test. The therapy of primary hyperparathyroidism consists in the early extirpation of the parathyroid tumor. In secondary hyperparathyroidism, treatment is determined by the type of primary disease.

Chronic Constipation.—At the same meeting Dr. K. Fellinger of Vienna pointed out that habitual constipation can be classified according to dynamic, localizing, or subjective complaints. The most frequent cause is the disturbance in the defecation reflex which in turn is often due to external or to psychogenic factors. Neurosympathetic disturbances, weakness of the abdominal muscles, and the posture during defecation may also play a part. Therapy should aim at the restoration of the automatism of the intestine, which is achieved most effectively by combination of drugs, roughage in the diet, gymnastics, and broad-spectrum antibiotics. The mode of action of this use of the broad-spectrum antibiotics in constipation is not fully understood. The maintenance of a therapeutic success is often more difficult than obtaining it. The cooperation of the patient is of vital importance. Dr. R. Scholz of Linz said that congenital megacolon is characterized by (1) the onset of symptoms immediately after birth, (2) demonstration of the narrow, aganglionic segment in the roentgenogram, and (3) histological demonstration of the absence of Auerbach's plexus in the narrow segment. The treatment of choice consists in the resection of the narrow segment. In contradistinction to congenital megacolon, the so-called idiopathic megacolon usually appears in the second year of life and represents a purely functional regulatory disturbance on a neurosympathetic basis. In some patients there

The items in these letters are contributed by regular correspondents in the various foreign countries.

is supposedly an inorganic deficiency of the autonomic plexus. In this condition conservative treatment is required.

Dr. A. Winkelbauer of Klagenfurt stated that, depending on the location and extension of the narrow aganglionic segment, an abdominal or perianal operation is performed on patients with congenital megacolon. He warned against extensive mobilization into the pelvis, because this may later result in fecal incontinence and impairment of sexual potency. Splanchnicectomy and sympathectomy have proved ineffective. Since 1950 favorable results have been obtained in patients with congenital megacolon with a method that resembles Heller's longitudinal splitting in patients with pylorospasm. Generally speaking, the wide use of surgical methods in patients with chronic constipation is decreasing, chiefly as the result of the efficacy of medical treatment. Dr. F. Brücke of Vienna said that in patients with habitual constipation, which is practically always colonic, the use of purgatives is probably indispensable but that they should be varied and used intermittently.

The Cervical Syndrome.—At the same meeting Dr. H. Hoff of Vienna said that the incidence of the cervical syndrome has been increasing. Isolated osteochondrosis is to be differentiated from other syndromes that are produced by changes in the cervical portion of the vertebral column such as disk hernia of the cervical column, scalenus syndrome, and cervical rib syndrome. The therapy of the isolated osteochondrosis of the cervical vertebral column consists in orthopedic measures, physical measures, muscular relaxants, exercise therapy, psychotherapy, and, with regard to the irritation of the sympathetic nerves, the administration of hydrogenized alkaloids of ergot. Dr. H. Kraus of Vienna recommended sympathectomy including the two upper thoracic ganglions in patients with severe cervical syndrome or with humeroscapular periarthritis. Cervical disk hernias are especially suitable for surgical treatment. Early operation is particularly urgent in the medial form because irreversible damage to the spinal cord will result quickly from compression of the anterior spinal artery. Operation on a lateral disk hernia is technically simpler and results in cure in about 50% of the patients. In patients with the scalenus syndrome the scalenus muscle is resected, but relapses frequently follow, probably as the result of a sympathetic component.

Copper and Iron.—At the same meeting Dr. E. Gisinger of Vienna said that it is customary to examine the iron, copper, and transferrin content of the serum. Transferrin is a specific serum protein that combines with iron. Normally only about 33% of the transferrin is saturated with iron. During pregnancy and the puerperium, serum iron and transferrin show no deviation from the normal whereas the copper content of the serum is greatly increased. Such an increase in the copper content of the serum is found otherwise only in the presence of malignant tumors, in the hemoblastoses, and in infections in which, however, there is in addition a significant decrease in the serum level of transferrin and iron. The iron content of the serum is also reduced in conditions accompanied by iron deficiency, but in these the transferrin level is greatly increased. This finding is ascertainable only in the presence of sideropenia. It is thus possible to confirm or disprove the presence of sideropenia by determining the serum iron content and the transferrin content in a single blood specimen. This is of great therapeutic interest because iron therapy is effective only in sideropenia, whereas anemia caused by infection or by a tumor remains uninfluenced thereby and is cured only after the primary disorder is corrected, and without additional hemopoietic therapy.

In hemochromatosis the transferrin is completely saturated with iron and the serum copper content is normal. Hepatitis differs from obstructive jaundice by a great increase in the serum iron level, whereas that of transferrin and copper are virtually normal. Obstructive jaundice is usually accompanied by a reduction in the serum iron and transferrin level, whereas the serum copper level is generally increased. The increased resorption of an iron preparation in iron deficiency states can be demonstrated photometrically and is even macroscopically visible by comparing the color of serum samples withdrawn before and three hours after its administration. The first serum specimen is pale green or yellow, whereas the second is orange. Investigations on the iron and copper metabolism are of prognostic significance, particularly during the cytostatic treatment of malignant diseases. Patients in whom the serum iron, transferrin, and copper levels became normal after treatment did not relapse for at least four months and generally much longer. Patients in whom these values did not become normal after treatment either received no therapeutic benefit or had a relapse within less than two months after the cessation of treatment.

Cardiac Surgery.—At the same meeting Dr. F. Lindner of Berlin pointed out that mitral stenosis is the commonest of all valvular lesions. The death rate from valvotomy is about 4%. Improvement in circulation and reduction of pulmonary pressure was obtained in 70% of the patients operated on, but in about 2% of these patients a residual stenosis must be expected. Results were less satisfactory in patients who underwent double valvotomy for combined aortic and mitral stenosis, but the results after this operation seemed to be better in these patients than in those with isolated aortic stenosis. The latter condition was frequently congenital. The

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postoperative death rate in these patients frequently reached 28%. For this reason operation is indicated only for circulatory insufficiency of vital organs (syncope and stenocardia). Uncomplicated pulmonary stenosis is rare. It is usually associated with other defects. The most frequent combination of defects are the tetralogy of Fallot. The death rate for this operation ranged between 7 and 15%, and many late deaths also occurred.

Portal Hypertension.—At the same meeting, Dr. H. Kalk of Kassel said that portal hypertension develops as the result of a circulatory obstruction in the region of the vascular systems of the liver, and, depending on the location of the obstruction, it is possible to differentiate between posthepatic, intrahepatic, and prehepatic blockage. Partial obstruction may result from thrombosis of the splenic vein. The pressure increase in these various forms of blockage may reach 800 mm. of water (normal range 50 to 200 mm.). This enormous pressure is to be explained by the entrance of arterial pressure by way of open anastomoses within the liver. The findings include meteorism, the formation of anastomoses and varices in the region of the abdominal wall and cardia ventriculi, and splenomegaly. Ascites develops in about 36% of these patients. The chief dangers of portal hypertension consist in the increasing protein deficiency as the result of the repeated tapping to remove the ascitic fluid and particularly the blood loss from the esophageal varices. The bleeding from the varices is the chief indication for a shunt operation which, however, should be carried out only if (1) one knows the exact cause of the disorder, (2) one knows of the location of the obstruction, and (3) the general condition of the patient and particularly that of his liver is such that survival is to be expected. Therefore patients in whom the serum protein level is less than 3 mg. per 100 cc. and the serum bilirubin level is more than 3 mg. per 100 cc. should not be operated on. Ascites alone does not constitute an indication for surgical treatment. With cautious evaluation of suitability for operation, shunt operations have a death rate of about 15%.

Dr. K. Herlyn, of Göttingen pointed out that (1) Talma's omentopexy has been practically abandoned, (2) operations on the esophagus and the spleen include ligation of the esophageal varices aimed at preventing congestive stasis of blood in the varices, (3) extirpation of the spleen is advisable only in the presence of thrombosis of the splenic vein and is attended by a relatively high death rate, and (4) shunt operations involve shunting of the blood of the portal vein into the vena cava either through a portacaval or a splenorenal anastomosis. Another method is the ligation of the hepatic artery which, however, has proved dangerous and relatively ineffective. Since the death rate of shunt operations is high, they are indicated only in patients with profuse hemorrhages from esophageal varices. Cessation of varicose bleeding is the most important criterion for the success of the operation.

Skin Cancer.—At the same meeting Dr. S. Tappeiner of Vienna said that skin cancer is the most frequent type of cancer in men, and in women it is third as regards frequency. Predisposing causes include chronic irritation, actinic and ionizing rays, and irritants that reach the skin by way of the blood stream, such as arsenic. Precancerous changes are especially frequent after contact with arsenic compounds. In regions with intensive solar radiations, carcinoma of the skin is four times as frequent as in other countries. Estrogens also have a cancerogenic effect and for this reason hormones should never be given without definite indications. The prophylaxis of skin cancer consists in the treatment of senile keratoses, keratoses induced by arsenic compounds, cornua cutanea, and leukoplakias.

Varicose Ulcer.—At the same meeting Dr. H. Rotter of Salzburg stated that the equilibrium between the inflow and outflow of the blood is impaired in varicose ulcers. The excess of fluid acts as a foreign body. It becomes encapsulated by connective tissue and in this way the palpable infiltrations characteristic of this lesion develop. As long as the deep veins still function, no infiltrations or ulcers develop, even if the veins are severely varicosed. The harder these infiltrations become the greater is the resistance to healing and the more readily a relapse occurs after the ulcer is closed. Complete healing is possible only after removal of these infiltrations. In order to achieve this, a foam rubber cushion is applied as a pressure bandage. This cushion acts as a buttress or a supporting wall between the leg and the bandage and mechanically leads to gradual dissolution of the infiltrations. The advantage of this treatment is that it permits the patient to be ambulatory.

Cancer of the Larynx.—At the same meeting, Dr. H. Blümlein of Erlangen said that carcinoma of the larynx has increased in recent years and that it is found almost exclusively in men. He believed that endogenous noxae could be excluded as causes, since a biological change that is found only in men can be excluded in the age group affected. Possible causes include such air pollutants as gaseous industrial wastes, products of tarring processes, and the exhaust gases of motor vehicles. It is believed, however, that these are secondary to the action of inhaled tobacco smoke. Dr. Riccabona of Vienna said that the decision whether to excise or irradiate a laryngeal cancer must be based on the conditions in each individual patient. In case of recurrence,

excision not irradiation is advisable. When irradiation is used the normal dose should not be exceeded because this is rarely effective and, should excision become necessary later, it would make the operation much more difficult. Whereas formerly irradiation was generally preferred for older persons, the trend is now toward excision because the short time involved in operation is better tolerated by elderly persons than is the long period involved in irradiation. Excision is preferred also in the presence of pulmonary tuberculosis, because during irradiation exacerbation of the tuberculosis may occur. Dr. L. Hörbst and E. Ruckensteiner of Innsbruck reported that after surgical removal of one wing of the thyroid cartilage in patients with laryngeal cancer they apply 10,000 to 20,000 r in divided doses in the course of two weeks. The removal of the thyroid cartilage does not damage the respiratory passages. This treatment was used in 48 patients of whom 37 were cured.

The Steinhof Mental Hospital.—At the meeting of the society of physicians in Vienna on Jan. 10, Dr. H. Hoff said that when Steinhof was completed in 1907 it had 5,200 beds and was the largest and most up-to-date institution for the insane in Europe, but the increase in population and the repeated use of some of the pavilions for other purposes gave rise to constant overcrowding. Now by virtue of insulin therapy and electric shock therapy many mental patients can be discharged, and this has given some relief. Modern psychiatric treatment aims at remissions or at least at readjustment of the patient to social life. The use of physical restraint is rapidly disappearing. The average duration of hospitalization of the mental patients in Steinhof has been shortened from 170 to 119 days. Dr. E. Novak and co-workers reported that there has been a marked reduction in the number of patients with progressive paralytic and epileptic diseases. The increase in longevity in the population and the higher standards of living which promote alcoholism have resulted in an increased number of patients with senile and alcoholic psychoses.

Idiocy.—At the same meeting Drs. H. Gross and E. Kaltenbäck reported on a series of 546 patients with extreme mental deficiency which was either congenital or acquired in the first three years of life. The largest group, consisting of those with sequelae of cerebral circulatory defects, mostly of perinatal origin, included 103 patients; 86 were idiots with negative findings (oligoencephalia); 82 had disturbances of cerebral development; 65 were mongolian idiots; 45 had idiopathic epilepsy; 34 had had infantile encephalititis and meningitis; 11 had thyrogenous idiocy; and 9 had disturbances of cerebral metabolism.

Modern Treatment of the Insane.—At the same meeting Dr. K. H. Boysen and co-workers reported on the treatment used in 1957 for the institutionalized insane. Insulin shock therapy cured 25% and brought about social remission in 59%. An average of 43 such treatments were given to those getting this therapy. Coma usually lasted about 41 hours. Electric shock therapy is the treatment of choice in patients with threatening catatonia. Pyretotherapy was used in patients with refractory chronic schizophrenia. Chlorpromazine was given to 150 patients with all forms of schizophrenia. Of these, 96 were cured and/or became socially well adjusted. Chlorpromazine was given in rapidly increasing doses up to 500 mg. per day, starting with injections and switching to suppositories and tablets. The maintenance dosage of eight tablets (200 mg.) was given for two or three months.

FRANCE

Mammary Cancer.—Bernard and Mathe (*Bulletin de l'Association française pour l'etude du cancer*) stated that in patients with mammary cancer cancerous cells are more numerous in the iliac than in the sternal marrow. These cells are dystrophic and present nuclear and cytoplasmic anomalies. They are more easily detected when they are piled up and less easily identified when they are alone. Indirectly syndromes of medullar fibrosis are found in the blood and the marrow. Marrow punctures appear to be anemic and may sometimes be white.

Nicotine Poisoning.—R. Lecocq (*La Vie Medicale*, June, 1957) said that patients with chronic nicotine poisoning show a latent polyneuritis and a chronic acidosis. Nicotine in the body produces a carboxyhemoglobinemia and destroys vitamin C. The author advises impregnating the buccal and laryngeal mucosa with a solution of silver proteinate (1% silver) to provoke disgust with smoking. To patients with acute nicotine poisoning he gives an intravenous injection of a glucose extract of tobacco or a solution of nicotine neutralized with ascorbic acid. For this treatment, the patient must go to the hospital. The results have been excellent.

Heparin for Tuberculous Patients.—Weil and Nehorai (*La Therapie*, vol. 3, 1957) have treated 300 tuberculous patients with heparin without observing any exacerbation of the disease or any hormonal imbalance. If caseous tubercles are present, they inject 1 to 2 ml. of heparin locally. The patient may recover within four or five weeks. They also give a dose of 50 to 100 mg. of heparin intravenously every day along with suitable antibiotics. No complications have occurred. They believe that heparin destroys the tubercle bacillus and facilitates the action of antibiotics.

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Alcoholic Cirrhosis.—Cachin and co-workers (*Archives des maladies de l'appareil digestif*, June, 1957) treated 50 patients with alcoholic cirrhosis with 20 to 50 mg. of deltacortisone daily for 20 to 90 days. Of these, 31 had mild ascites; 14, severe ascites; and 5, no ascites. Other treatment was eliminated or reduced to a minimum. The patients noted a marked general improvement. In 24, good diuresis was obtained and in 25 the ascites and edema disappeared; 22 of the patients with ascites were able to leave the hospital. Of the 14 with severe ascites, 8 died.

Herpes Zoster.—Vegas and Vegas (*Annales de dermatologie et de syphilographie*, August, 1957) gave 20 to 60 mg. of emetine hydrochloride subcutaneously every day for a maximum of five days to 31 patients with herpes zoster. In 30 of these the treatment was successful. The progress of the disease was checked after the first or second injection, and the pain disappeared in 12 to 72 hours.

Operation for Male Sterility.—In the Entretiens de Bichat held in October, H. Bayle reported the results of operation in 184 sterile men. In 40 a latero-lateral epididymodeferential anastomosis was impossible. Since the operation, 31 couples have had 46 children. Epididymal puncture or deferentography should not be performed. The author performed a second operation on some in whom the first had failed, and in seven of these success was achieved.

PERU

Occupational Health.—The first seminar on occupational health, organized by the Institute of Occupational Health of the Ministry of Public Health and Social Welfare, under the auspices of the Office of International Cooperation of the United States and the Pan-American Sanitary Office, was held in Lima in January. In the reorganization of the Ministry of Public Health in June, 1957, the Department of Industrial Hygiene was renamed Institute of Occupational Health. Dr. Ramón Vallenas, Director of the Institute, said that thus far its principal activities are (1) to evaluate the occupational health problem, (2) to furnish technical consultation, (3) to make medicolegal examinations, and (4) to train professional and technical personnel. Although at first the institute directed most of its attention to mining industries, it now looks into all types of industrial work. Dr. M. Espinoza, stated that the occupational health problem comprises two phases: an examination of the worker and an examination of his environment at work and at home. In a series of 9,466 workers, mostly miners, the most important abnormal findings were caries in 49.5%, pyorrhea in 27%, conjunctivitis in 21.5%, pterygium in 20.3%, myopia in 14.3%, endemic goiter in 4.3%, deviation of the nasal septum in 3.1%, and miscellaneous in 8%. Disorders of the digestive tract and genital organs were rare. Roentgenograms of the chest in a group of 14,634 miners revealed silicosis in 4.8%. Tuberculosis was present in 0.9%.

C. Maher, an engineer, presented statistics to show that when there are less than 4 million dust particles per cubic foot of air silicosis will not develop. The incidence of silicosis increases with an increase in the concentration of dust particles above this level and with the duration of exposure. Between January and June, 1952, Dr. J. Ferrándiz studied the occupational risks in 396 industrial centers and found that 47,757 of the 66,372 workers involved were exposed to potential risks; 24.2% were exposed to organic dusts, 24.4% to metals other than lead, 20% to silex dust, 17.1% to substances known to produce dermatitis, 14.4% to lead and its compounds, 15.2% to organic solvents, and 7.8% to sudden temperature changes or very loud noises. Little effort was made to control these hazards. The commonest means of control consisted in protective clothes (rubber boots and gloves).

The Institute of Occupational Health has thus far chiefly studied occupational diseases in miners. Pneumoconiosis was by far the principal health problem among these people. Dr. Ferrándiz found silicosis in 5.3% of a series of 17,401 workers in 37 mining centers. The average time spent in the mines by these victims was 10.7 years. The average time spent in the mines by those without silicosis was 5.5 years. On the other hand, no cases of silicosis were found in laborers in a cement factory. Of the 1,468 workers in a foundry, 9.4% were found to have chronic lead poisoning and 16.8% to have an abnormally high lead absorption, the minimal duration of exposure in both groups being 30 days. Chronic lead poisoning was also found in 40.2% of the workers in five storage battery factories. About 6% of the workers in glass factories were found to have severe pulmonary fibrosis; 6.5% of those in dye factories, on the other hand, had contact dermatitis, as did 5% of the workers in tanneries.

Dr. O. A. Sander of the United States said that in his country the annual number of new cases of silicosis has decreased markedly in recent years as a result of the increasing attention given to dust control, particularly in foundries. He warned that siderosis may be mistaken for silicosis, especially by inexperienced physicians. The diagnosis is based on history, roentgenograms of the chest, and laboratory findings. In the roentgenogram, a fine discrete stippling throughout both lungs is usually seen in siderosis, the hilar shadows appearing normal; whereas in silicosis the nodules are larger, vary in size, and are unevenly distributed, the hilar shadows being particularly increased in size and density because of the existence of enlarged, fibrotic,

silicotic lymph nodes. Silicosis associated with siderosis may give radiologic findings indistinguishable from those seen in pure silicosis. Siderosis does not produce incapacity for work and does not increase the susceptibility to tuberculosis. Patients with silicosis, however, may eventually be forced to look for another type of work. Although silicosis predisposes the patient to tuberculosis, whether this disease develops or not depends on the prevalence of tuberculosis in the region where the worker lives.

Dr. J. Zárate Polo stated that along the Peruvian coast 406 cases of poisoning by pesticides were reported from 1952 to 1957. The actual number was probably much greater, as many cases were not reported or were misdiagnosed. Of the 406 cases, 35 patients or 8.6% died. Insecticides containing phosphorus accounted for the largest number—172 or 42.4%; those containing arsenic, for 46 or 11.3%; those containing chlorine alone or with phosphorus, for 37 or 9.1%; those containing miscellaneous poisons, for 100 or 24.7%; and in 51 cases, or 12.5%, the type of insecticide could not be determined.

Dr. C. A. Carlin inspected the environmental conditions in 22 mines and examined 11,684 workmen. Grouping the mines according to the content of free silica in the air, it was found that in those where this accounted for less than 5% of the dust particles present with an average of 6,900,000 dust particles per cubic foot of air, the incidence of silicosis was 0.26% for subjects exposed to the environment five years or less. This percentage rose to 3.09% in those exposed for 5 to 14.9 years. In mines where the proportion of free silica ranged between 5 and 49.9%, the incidence of silicosis was 1.16, 8.16, and 14.40%, respectively, for those exposed for less than 5 years, 5 to 14.9 years, and 15 years or more respectively. In mines where the concentration of silica was 50% or greater, the average concentration of dust particles per cubic foot of air being 4,800,000, the incidence of silicosis was 3.07, 4.83, and 7.69%, respectively, for groups with the exposures listed. On the other hand, grouping the mines according to the dust concentration in millions of particles per cubic foot of air, it was shown that in those where such a concentration was less than 5 million particles the incidence of silicosis was 9.30, 6.15, and 12.97%, respectively, for the three groups. If the concentration of dust was between 5,000,000 and 19,900,000 particles, the incidence was 1.83%, 9.82%, and 15.49%, respectively, and if the dust concentration was greater than 20 million particles, the incidence was 3.50, 5.03, and 10.17% respectively. Of 7,212 workers examined whose exposure ranged from 0 to 4 years, 94 or 1.3% were found to be affected with silicosis. Dr. J. G. González said that pneumoconiosis is a general term indicating retention of dust by the lungs, but not implying pulmonary disease. The pneumoconioses may therefore be divided into benign and incapacitating. The first group includes siderosis, stannosis, anthracosis, and baritosis; the second includes asbestosis and silicosis.

Physicians and Bureaucracy.—A recently enacted law prohibits receiving two or more paychecks from the state with the exception of those derived from teaching. This has caused serious trouble in the Peruvian Medical Federation. The decree, made principally to prevent the monopoly of state posts and to secure a better distribution of the bureaucratic positions, will compel many physicians having several public appointments to retain but one of them. This act is being resisted by most of the affected physicians. Nevertheless many of them, especially the younger ones, favor the law as it will enable more of them to obtain government jobs. Recently graduated physicians were confronted with a shortage of positions. It is proposed that an exception be made and that one or more part-time positions be permitted unless there is an incompatibility in the hours of work.

UNITED KINGDOM

Dust from Cement Works.—The concentration of cement works along the Thames is the biggest in the country. There are frequent complaints from the local inhabitants about the gray dust that pervades the area and is believed to emanate mainly from the chimneys of the cement works. Dr. J. H. Hudson (*M. Officer* 98:351, 1957) investigated the possible health hazards and was unable to find any direct evidence of harm to human health. He even suggested that the dust may in some respects be beneficial. In this area, cement is made from chalk and clay, and since 1945 the manufacturers have spent 2.8 million dollars on dust control. Apparently, however, even the best of these is only 98% effective. Dr. Hudson's most interesting finding is that the incidence of lung cancer in the cement districts is markedly lower than that of Greater London, their close neighbor. Thus, the standardized mortality ratio for these districts is only 93, compared with 132 for Greater London. Furthermore, in spite of the fact that the cement districts have a population of 150,000, their death rate from respiratory diseases is that of a population of 50,000, although so far as this country is concerned, death rates from respiratory diseases tend to increase with the degree of urbanization.

Mass x-ray records of population in cement districts show no greater evidence of respiratory disease than is to be expected in an industrial district. A comparison of the incidence of catarrhal infections, including bronchitis, in 232 pupils at a school

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near the cement works, with a similar number attending schools four miles away, showed no appreciable difference. Dr. Hudson points out that in industrial towns it is the combination of the sulfur dioxide with the complex contents of smoke particles that damages lung tissues. At the Central London power station, sulfur dioxide is removed from the flue gases by chalk and lime. Dr. Hudson believes that in the cement districts the chalk and lime suspended in the air may neutralize the acid oxides of sulfur and thereby prevent their harmful effects.

Cerebral Palsy.—A survey of cerebral palsy among children in the county of London, by Murdoch McGregor and co-workers (*M. Officer* 98:367, 1957), revealed an incidence of 1.18 per 1,000 among children aged 5 to 14, and of 1.04 among those aged 0 to 14. Of the 722 children with palsy aged 0 to 16, 483 had spastic paralysis, 58 athetosis, 46 ataxia, and 78 had two or more types of handicap. About 33% of the children (243 of 722) had no handicap other than limb involvement, another 33% had one additional handicap, and the remainder had more than one handicap. Whereas 40% of those with spastic paralysis had no handicap other than limb involvement, only 21% of those with athetosis and 22% of those with ataxia were free from additional handicaps. The other most common defects were speech defects in 261, ineducability in 193, and epilepsy in 109 patients. Only about 5% (35 patients) were reported as having hearing defects. Birth weights were available for 518 of the children; of these children, 179 (34.6%) weighed 5½ lb. or less at birth, compared with 7% for all births. Examination of the educational attainment of the children receiving education suggested that the children with cerebral palsy were not rising to the level made possible by their intellectual ability. No insurmountable difficulty arose in finding employment for most of these children when they left school.

Food Poisoning due to Zinc.—Eight outbreaks of food poisoning due to zinc occurred in England and Wales in the 15-year period, 1942 to 1956. An analysis of these (*Monthly Bull. Ministry of Health* 16: 241, 1957) reveals that in all cases in which it was accurately determined, the interval from ingestion to onset of symptoms ranged from within 10 minutes to within 3 hours. The symptoms were mainly vomiting, with or without nausea, and recovery was rapid. Four of the outbreaks were associated with stewed apple rings, two with bilberry juice, one with rhubarb tart, and one with mashed potatoes. Mashed potatoes were described as an unexpected vehicle in zinc food poisoning, and the amount of zinc in the potatoes examined was low—only 31 ppm, but the association was definite, and the conclusion reached was that the sample examined was not representative of the potatoes eaten. The source of the zinc in all seven outbreaks, for which information was available, was the galvanized container in which the food had been soaked, cooked, or stored after it was cooked. The amount of zinc found in the food ranged from 31 to 5,000 ppm, but was mainly between 200 and 1,500. Although some contend that so-called zinc poisoning is due to lead, since lead is present in most zinc coatings, in one of the outbreaks no lead, copper, or arsenic was detected and in another no lead, copper or cadmium was detected. In these two, at least, lead was not the cause of the symptoms; and though the records of the other outbreaks do not specifically state that other metals were not found it is known that they were looked for in some and possibly in all.

Disciplinary Action.—In 1956, recommendations were reported by executive committees to the Minister of Health in 1,384 cases involving allegations that physicians, dentists, pharmacists, or opticians had failed to comply with their terms of service. This was 96 less than in 1955. As a result of these recommendations, one physician resigned from the health service, and money was withheld from 45 physicians, 67 dentists, 188 pharmacists, and 9 opticians. Warning letters were sent to 352 physicians, other action was taken in 126 cases, and no action in 604 cases.

Artificial Insemination is Not Adultery.—Artificial insemination from a donor is not adultery as the law of Scotland now stands, according to a judgment given in Edinburgh. The case was one in which the husband sued for divorce on the grounds that his wife, now resident in New York, had a child as the result of artificial insemination through a donor, without the agreement, or indeed the knowledge, of her husband. The judge said that there were grave moral, ethical, social, and personal considerations involved in the practice of artificial insemination in its various forms, but that the question to be determined was not the moral culpability of such an act, but whether it constituted adultery in its legal meaning. The idea that adultery might be committed by a woman alone in the privacy of her bedroom, aided and abetted only by a syringe, is one with which the earlier jurist had no occasion to wrestle. Certainly, this form of perpetuation of the species does not conform to the common conception

of adultery. Having studied all the available evidence, the judge concluded that artificial insemination did not come within the definition of sexual intercourse as commonly understood.

Death After Self-Injection.—The death of a physician aged 36, after he had injected himself with penicillin, was the subject of an inquest at Wakefield (*Brit. M. J.*, Dec. 7). The pathologist found that the cause of death was anaphylactic shock. He observed signs of early acute bronchitis, and it was possible that the physician had taken penicillin for that condition, a normal thing for a medical man to do. An empty vial found in his room had contained penicillin, and there was a hypodermic mark on his thigh. The doctor's landlady hearing his call for help had summoned another doctor who on his arrival found that the patient was unconscious. He died in spite of efforts to revive him.

Poliomyelitis Vaccine.—Two extensions to Glaxo Laboratories' poliomyelitis vaccine production unit were opened in November. With the extra capacity the company hopes to raise its production of poliomyelitis vaccine by 50% by early summer. The extensions consist of a 10,000 sq. ft. safety-testing suite and a second animal house. The larger of the two buildings is being used for preparation of the synthetic medium on which the tissue cultures are propagated, preparation and maintenance of the monkey-kidney tissue cultures, and safety-testing of both the single-strain vaccine pools and the final trivalent vaccine. The new animal house is designed for safety-testing the vaccine in vivo under sterile conditions. The space in the main production laboratories gained by this new scheme will be used for increasing the output of the vaccine pools.

Antithyroid Activity of New Sedative.—A new sedative, N-phthalyl glutamic acid imide, is being extensively used in Europe as a sedative and hypnotic. It was synthesized in Germany in a search for a drug combining the advantages of the barbiturates without their undesirable side-effects. Claims have been made that the drug is virtually nontoxic and that no ill-effects have followed its prolonged administration to animals. Murdoch and Campbell (*Brit. M. J.* 1:84, 1958) found that it has an antithyroid action in man. This was ascertained by using I^{131}, in the following way: when thyroid activity, measured by a radioactive counting technique, was determined after administration of I^{131} and the results plotted against the square root of time, a linear graph was obtained over the first 10 hours. This standard graph was compared with one obtained after the new drug was given in doses of 50 to 400 mg. to euthyroid subjects. The results showed that in doses of 200 mg. or more the drug had definite antithyroid activity. It should therefore not be used for long-term sedation or hypnotic therapy, pending the results of a more detailed study. Its mode of action on the thyroid is unknown.

Transmission of Staphylococcus.—Hare and Ridley (*Brit. M. J.* 1:69, 1958, examined the skin and clothing and nasal carriers of Staphylococcus pyogenes var. aureus and showed that about 60% of the carriers have enough organisms on certain areas, particularly their hands and clothing of the anterior part of the body, to enable them to transmit these organisms to other persons with whom they come into direct physical contact. Transfer also occurs by means of such objects as blankets or towels that the carrier has handled, or by dispersal from the contaminated objects into the air during movement or shaking. Although with most of the carriers staphylococci were found in the nose, the number of organisms on nasal swabs gave little indication of the extent of skin and clothing contamination or of the ability to disperse organisms. Evidence was obtained that some apparently normal persons may harbor Staph. aureus on the skin of the perineum, and yet have none in the nose, or, if they have, they may be of a different phage pattern. It is thus evident that it is no longer justifiable to assume that only nasal carriers need to be considered when tracing the source of infection in hospital epidemics.

Cook and co-workers (*Brit. M. J.* 1:76, 1958) investigated the usual routes of spread of Staph. aureus in the newborn in nurseries. Of the 53 babies examined, all were found to be nasal carriers by the 10th day of life. The majority also carried staphylococci in their stools. Examination of bedding showed that this was not the immediate source of infection, and the provision of nursing staff with gowns and hand cream containing the antiseptic, chlorohexidine, made little difference to the extent of infection in the infants, but the application to the navel of a triple dye (brilliant green, 2.29 Gm.; proflavine hemisulfate, 1.14 Gm.; and crystal violet, 2.29 Gm. in 1,000 ml. of water) and the provision of individual gowns for each baby did reduce the nasal transmission rate on the 12th day by 25 to 30%. This suggested that the umbilical cord is a breeding ground for staphylococci. The authors believed that about 75% of the babies acquired their staphylococci from sources other than their attendants.

CORRESPONDENCE

ARTIFICIAL ORGANS

To the Editor:—In view of the recent creation of the Society for Artificial Organs, I believe the enclosed photograph of an early 19th century anonymous caricature taken from E. Fuch's "Die Frau

in der Karikatur" (Munich, Germany, Albert Langen, 1906) should prove interesting. The artificial buttocks, especially, are new to me.

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CHANCE

To the Editor:—In the Correspondence section of The Journal on Nov. 30, 1957, page 1739, appeared a letter from Dr. Ernest B. Zeisler of Chicago in which he offered criticism of my paper on "Treatment of Chronic Schizophrenia" which appeared in The Journal on Sept. 28, 1957. He noted that the fourfold table was not included in the paper, disagreed with my statement about the relationship of p values and establishment of a hypothesis, and quotes an example from a game of bridge to elucidate the problem for nonmathematical readers.

I must agree that my statement "a p value of less than 0.05 is adequate to establish a hypothesis" is incorrect. However, Dr. Zeisler's further comment that the p value cannot measure the probability that a hypothesis is correct and his discussion of the relationship of the p value and chi-square is erroneous. In my paper, the p value of 0.0003 means that 3 times out of 10,000 times it is possible by chance alone that the observed improvement found with azacyclonol can differ as much from the observed improvement seen after the placebo. Since three times out of 10,000 is exceedingly rare, chances are that the observed difference is due not to chance but to the therapeutic effects of azacyclonol.

The fourfold table used in the analysis is as follows:

	Improved	Not Improved	Total
Azacyclonol	61	110	171
Placebo	28	143	171
Totals	89	253	342

The above table combines the patients of group I and group II. For analysis of groups I and II separately, the fourfold tables would be as follows:

Group I

	Improved	Not Improved	Total
Azacyclonol	37	48	85
Placebo	15	70	85
Totals	52	118	170

Chi-square=8.5 and p=less than 0.01 and more than 0.001.

Group II

	Improved	Not Improved	Total
Azacyclonol	24	62	86
Placebo	13	73	86
Totals	37	135	172

Chi-square=3.4 and p=less than 0.1 and more than 0.05.

As to be expected, by analyzing the smaller groups the p value will increase, but the trend is the same in both groups.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Injury to Recurrent Laryngeal Nerve: Res Ipsa Loquitur.—The plaintiff filed suit for damages resulting from the alleged negligence of the defendant surgeon in the performance of a thyroidectomy. From a judgment of nonsuit in favor of the defendant, the plaintiff appealed to the district court of appeals, second district, division 2, California.

During an examination, the defendant noticed a nodule on the plaintiff's neck. It was his opinion that this was a premalignant lesion and that it was a serious condition. He advised surgery. Accordingly, the plaintiff entered the hospital on Sept. 30, 1952, for a thyroidectomy. She was examined by a medical student, who made notations on her hospital record concerning her physical examination and case history. The defendant testified, however, that he did not rely on this record in performing the operation. Before the operation, at the request of the defendant, Dr. Pies visited the plaintiff and examined her vocal cords. He found them to be normal in appearance and mobility. After the operation, the plaintiff's left vocal cord became totally paralyzed.

The plaintiff claimed negligence on the part of the defendant upon two theories: 1. He was negligent in his diagnosis that the plaintiff needed the operation. 2. He was negligent in the performing of the operation. The court said that there was insufficient evidence to support the plaintiff's first theory.

In support of the second theory, the plaintiff introduced extensive evidence tending to show that the defendant might have severed the recurrent laryngeal nerve during the operation. Since all the experts were of the opinion that this nerve should not be severed during the type of operation performed, said the court, a severance of that nerve would indicate that the doctor failed to exercise reasonable care in performing the operation. In an appeal from a judgment of nonsuit, however, said the court, all doubtful questions must be resolved in favor of the plaintiff. Therefore, if there was sufficient evidence indicating that the defendant did sever the nerve, then the case should have been allowed to go to the jury.

One of the plaintiff's experts was of the opinion that "there was undoubtedly some connection between the surgery and . . . the paralysis of the vocal cord." Another was of the opinion that the recurrent laryngeal nerve had been "severed or cut in half" in surgery. Both of these doctors had first examined the plaintiff many months after the operation and found a total impairment of the left vocal cord at that time, and both agreed that severance of the recurrent laryngeal nerve would produce immediate paralysis of the vocal cord, so that even partial movement of the cord after the operation would be inconsistent with a finding that the nerve had been severed. Dr. Pies, the plaintiff's own witness, testified that he had examined the plaintiff two days after the operation and that he found only a partial impairment of the cord at that time. The plaintiff denied seeing him until more than a month after the operation, however. Since all doubtful questions must be resolved in favor of the plaintiff, said the court, this conflict must be disregarded. The court also noted that the defendant had told the plaintiff after the operation that he was "sorry that it happened, he may have cut a nerve, because the nerves are very little. When you start to do anything it may happen in a thing like that." On the basis of all this evidence, the court of appeals was of the opinion that the case should have been submitted to the jury. The court also held that the case should have been submitted to jury with appropriate instructions showing the applicability of the doctrine of res ipsa loquitur.

Among other things, the plaintiff had also contended that Doctor Pies was an agent or employee of the defendant and that the plaintiff should have been permitted to examine that witness "as if under cross-examination." The court pointed out that Dr. Pies was called in by the defendant to examine the plaintiff before the operation. The record discloses no connection whatsoever between Dr. Pies and the hospital, so he was clearly not the agent or employee of the hospital. Nor does he appear to have been an agent or employee of the defendant. The fact that he was called in by the defendant and the fact that he and the defendant referred many cases to each other do not in themselves establish an agency or employee relationship. It does not appear that the defendant compensated Dr. Pies for his services. Dr. Pies was not subject to the defendant's control during the examination he made of the plaintiff nor did he say or do anything that would permit the plaintiff to assume that he was the agent or employee of the defendant. The relationship between one physician and another who is called in on a case by the former is typically that of independent contractor.

The judgment in favor of the defendant physician was reversed and the case remanded for a new trial. *Mayers* v. *Litow*, 316 P(2) 351 (California, 1957).

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ILLUSTRATED FILM REVIEWS

Illustrated reviews of current films, a regular feature in THE JOURNAL, *consist of an introduction by the author followed by a pictorial digest of actual frame enlargements selected as key points of the film.*

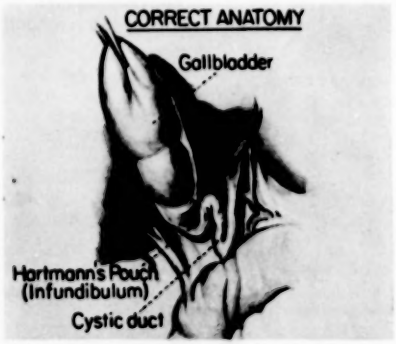
RALPH P. CREER, *Director*
Motion Pictures and Medical Television,
Council on Scientific Assembly.

INCOMPLETE CHOLECYSTECTOMY

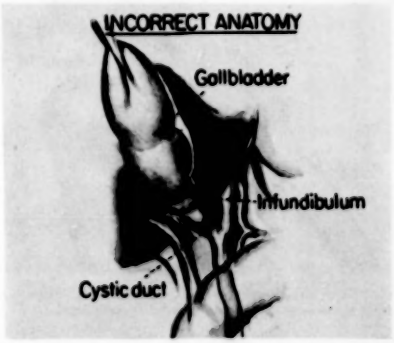
Philip Thorek, M.D., Chicago

Incomplete gallbladder surgery usually results from poor exposure, poor anesthesia, misconception of the surgical anatomy, and/or an attempt to perform a cholecystectomy in the presence of a fulminating acute cholecystitis. The differential diagnosis of incomplete cholecystectomy includes overlooked stones in the cystic or common ducts, spasm of the sphincter of Oddi, subacute and chronic pancreatitis, and, oddly enough, esophageal hiatus hernia. Symptoms are likely to recur if a pathological gallbladder is not removed completely.

The complaints of such a patient closely resemble those which were present prior to the cholecystectomy. That portion of the gallbladder which the surgeon may fail to remove is Hartmann's pouch (infundibulum). The latter is not to be confused with a cystic duct remnant. The human gallbladder does not have the ability to regenerate. One wonders if many so-called "cystic duct syndromes" or "post cholecystectomy syndromes" are not in reality incomplete cholecystectomies. Amputation neuromas along the cystic duct seem to be a rather farfetched possibility as a cause of post cholecystectomy pain. With the advent of the new hyperconcentrated gallbladder dyes the roentgenographic diagnosis of incomplete cholecystectomy can be made easily if the clinician keeps this not uncommon possibility in mind. The diagnosis is often missed because the history and he pathologist's report imply that the gallbladder was removed. The written review of this film appeared in THE JOURNAL, April 20, 1957, page 556.



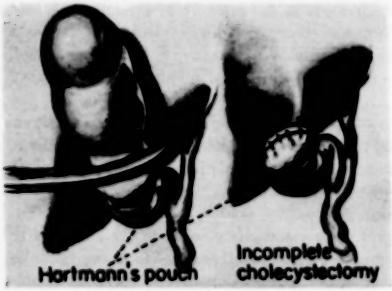
1. Hartmann's pouch (infundibulum of the gallbladder) runs parallel to cystic duct before entering it.



2. This representation fails to show correct anatomic relationship between infundibulum and cystic duct.

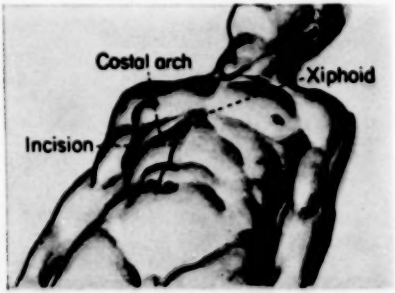
3. Cholecystoduodenal ligament, right extremity of lesser omentum, holds Hartmann's pouch down towards duodenum.

4. Anterior to Foramen of Winslow is hepatic trinity (common duct, portal vein, and hepatic artery).



5. If anatomy of Hartmann's pouch is not understood, pouch may be left behind in course of cholecystectomy.

6. Roentgenogram (with hyperconcentrated dye) after cholecystectomy reveals retained Hartmann's pouch.



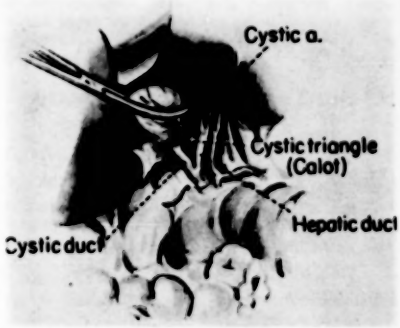
7. Long, muscle-splitting rectus incision is used, extending from xiphocostal angle to an inch below umbilicus.

8. Hartmann's pouch usually appears as slight bulging mass enmeshed in postoperative adhesions.

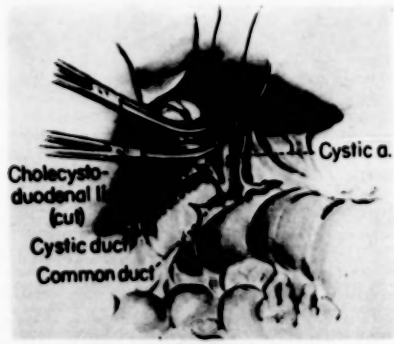
9. Lysis of adhesions will expose Hartmann's pouch.

10. Upward traction on pouch and downward traction on duodenum reveals severed cholecystoduodenal ligament.

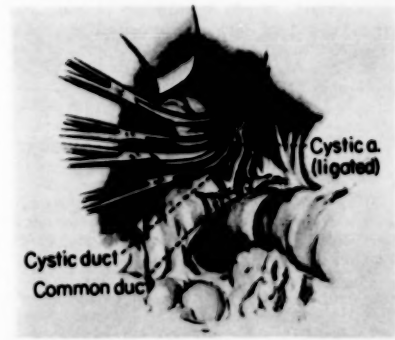
11. Blunt dissection breaks down cholecystoduodenal ligament and exposes ducts and vessels.



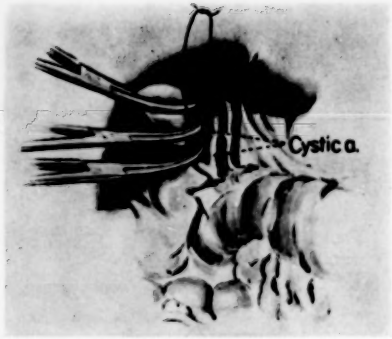
12. Calot's triangle should be exposed. It is bounded by cystic artery, cystic duct, and hepatic duct.



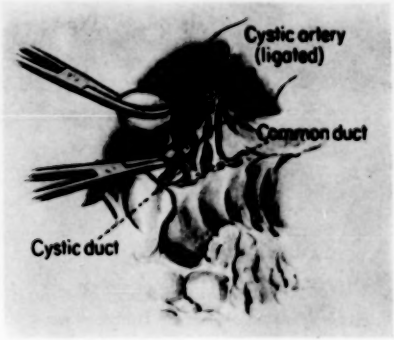
13. Cystic artery should be ligated prior to clamping and cutting whenever possible.



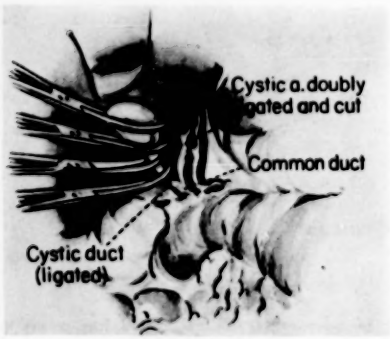
14. Cystic artery is divided between two right angle clamps placed above ligature.



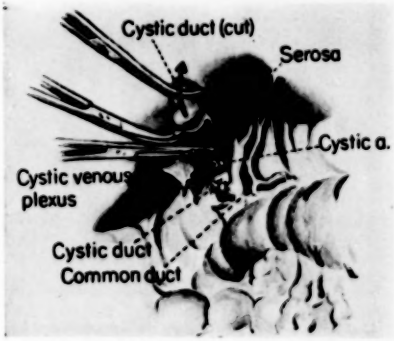
15. Second ligature is placed on cystic artery.



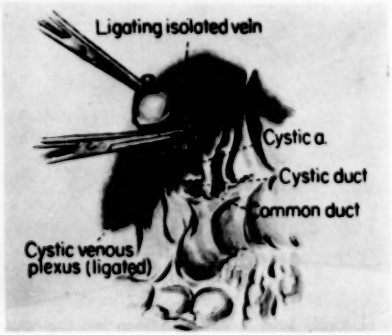
16. Cystic duct is ligated 0.25 in. from common duct.



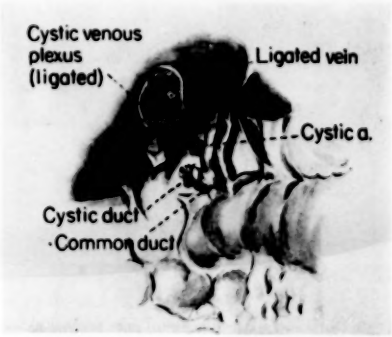
17. Cystic duct is clamped and divided above previously placed ligature.



18. No cystic vein accompanies cystic artery, only venous plexus, ligated separately.



19. Hartmann's pouch is removed from below upwards. Accessory ducts and veins draining into liver bed are ligated separately.



20. Completed operation.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Pulmonary Emphysema. E. Wenk. München. med. Wchnschr. 99:1851-1857 (Dec. 6) 1957 (In German) [Munich, Germany].

The author calls attention to the fact that some physicians have the habit of using the terminology of their patients, particularly with regard to "asthma," applying this term to practically any condition accompanied by dyspnea. He found that of 220 patients who were hospitalized with signs of pulmonary emphysema, 54 had been referred with a diagnosis of asthma or bronchial asthma; a diagnosis of various types of heart lesions, including cardiac asthma, had been made in 67, and emphysema had been diagnosed in only 35 patients. In the remaining patients, pneumonia, bronchitis, influenza, and various other conditions had been diagnosed, and in some patients no diagnosis had been made. The most prominent symptoms of emphysema are dyspnea, cyanosis, and thoracic rigidity usually in the inspiratory position. Later there may be signs of cardiac insufficiency, which may lead to death. Emphysema is a disease of the more advanced age groups, all but 7 of the patients being over 40 years of age. Of a total of 230 patients observed over a period of 15 years, all but 33 were men. This total number might suggest that emphysema is relatively infrequent, but these were only rather severe cases in which clinical therapy proved necessary. In the practice of an internist, 38 patients (2.3%) with emphysema were observed among 1,683 patients. The evaluation of chest roentgenograms revealed 423 patients (4.2%) with signs of emphysema among a total of 10,106.

Two forms of emphysema have been differentiated: (1) the vesicular and (2) the interlobar or interstitial. Although allergy of the respiratory organs may cause reversible emphysema, processes involved in physical aging play a part in the majority of patients. The fact that several cases may occur in a family suggests a hereditary predisposition. Occupational factors should therefore not be overemphasized, since certain occupations (glass blowing, stone-cutting and musical work) also run in families. A false respiratory technique and certain predisposing disorders may play a part. The author lists important symptoms and laboratory findings, particularly hemoglobin values, blood sedimentation rate, eosinophil count, Takata-Ara reaction, electrocardiographic and respiratory changes, and circumference of the chest and vital capacity. Autopsy was performed in 9 of the 38 patients who died, and the reports were repetitious in the description of the emphysematous changes in the lungs. A suppurating bronchitis was mentioned in some. Size and weight of the heart were usually increased.

Clinical Course and Corticosteroid Excretion of Patients with Rheumatoid Arthritis During Long-Term Treatment with Corticotropin. O. Savage, P. Davis, L. Chapman and others. Brit. M. J. 2:1257-1262 (Nov. 30) 1957 [London].

The authors report on 49 patients with severe rheumatoid arthritis who were given long-term treatment with self-injected corticotropin (ACTH) and in whom regular clinical and biochemical observations were made for at least 6 months and up to 2½ years. Clinical suppression of rheumatoid arthritis was assessed by the tenderness of selected joints to firm pressure, by measuring the strength of grip with an ordinary sphygmomanometer and by determination of erythrocyte sedimentation rate. Estimation of the urinary excretion of total 17-hydroxycorticosteroid was done by Norymberski's method weekly throughout treatment and more often during the initial stages; it was carried out from the start of the treatment in 41 patients. Six of the 49 patients went into remission, 35 are still receiving corticotropin therapy, 1 died, and the therapy was discontinued because of side-effects in 6 and because of apparent resistance to corticotropin in 1.

In each of the 41 patients suppression of activity of the disease as indicated by a significant diminution of joint tenderness, increase in the strength of the grip, and a fall in the erythrocyte sedimentation rate occurred after the administration of corticotropin in a dose which proved sufficient to raise the urinary excretion of 17-hydroxycorticosteroid by a significant amount. The excretion was doubled in 24 patients, and it was increased by more than 50% in 17. There was not a single patient in whom

The place of publication of the periodicals appears in brackets preceding each abstract.

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clinical suppression of the disease was not accompanied by a significant increase in corticosteroid excretion. After the initial response, the dosage had to be adapted to the fluctuation of the activity of the disease or the development of an altered sensitivity to the hormone. It was not necessary to maintain a high level of adrenal stimulation in order to obtain continued clinical improvement, and adequate clinical and biochemical response could be maintained for years with only minor adjustments of steroid dosage. The occurrence of remission was recognized when during a period of satisfactory clinical response a fall in the patient's 17-hydroxycorticosteroid excretion was noted without any concurrent relapse of the disease. The more severe side-effects, such as hypertension and glycosuria, occurred only when a high level of hydroxycorticosteroid excretion had existed for some weeks, and they were reversible. Androgenic side-effects, particularly acne, occurred commonly in women before the menopause with only slight adrenal stimulation. The absence of dyspepsia in the patients was impressive. A peptic ulcer occurred in only 1 patient, but gastric or duodenal ulcers occurred in 13 of 83 consecutive patients who were given steroids orally during the past 5 years. If corticotropin was withdrawn, relapse of the arthritis followed, but this was not accompanied by the distressing general symptoms which attended the withdrawal of cortisone and other orally administered steroids.

Treatment of severe rheumatoid arthritis with self-injected corticotropin over long periods is a practical procedure and, when used with biochemical estimations, has certain advantages over oral administration of cortisone and its newer analogues. Biochemical control during long-term treatment of patients with severe rheumatoid arthritis with corticotropin results in a more accurate and less dangerous dosage regimen than was formerly practicable. Although the use of steroid therapy will probably not alter the basic course of the disease, the satisfactory suppression of the inflammatory element will, however, enable the patient to regain independence and live a normal life.

Ardmore Disease. W. L. Wilson, C. D. Williams, S. L. Sanders and R. P. Warner. A. M. A. Arch. Int. Med. 100:943-950 (Dec.) 1957 [Chicago].

The authors report on the outbreak and course of a highly infectious epidemic disease which occurred at Ardmore Air Force Base, Okla., in the fall of 1955. The disease is characterized by upper respiratory infection, prolonged malaise, generalized adenopathy, painful hepatosplenomegaly, and a pronounced tendency to relapse into a chronic smouldering illness of several months' duration. The clinical course superficially resembled that of infectious mononucleosis or infectious hepatitis, with some aspects reminiscent of epidemic pleurodynia. All of these diagnoses were considered originally but later rejected in view of the clinical course of over 100 patients. The notable differentiating points were the absence of jaundice, consistently negative heterophil agglutinations, and the absence of atypical lymphocytes. The authors believe that this syndrome represents a clinical entity which, in sporadic form, may go unrecognized or be erroneously diagnosed as infectious mononucleosis or anicteric hepatitis. It is referred to as "Ardmore disease," since an etiological designation is not possible. The authors feel that this is a definite and distinct clinical entity in spite of the fact that at present there is not a specific diagnostic test available.

The Clinical Course of Acute Renal Failure: Observations on 54 Cases. R. A. Palmer and E. W. Henry. Canad. M. A. J. 77:1078-1084 (Dec. 15) 1957 [Toronto].

The management of 54 patients with acute renal failure and the importance of blood dialysis in selected cases was discussed earlier. This report summarizes observations on the clinical features of the disease. The renal failure was due in 53 of the patients to acute nephrosis (ischemic and nephrotoxic) and in 1 to acute glomerulonephritis. Approximately two-thirds of the cases were classified as ischemic nephrosis and about half of these arose out of obstetric complications. Approximately one-third of the total group are classified as nephrotoxic nephrosis, the main etiological factor being carbon tetrachloride. Acute alcoholism was an apparent cause in 3 of the cases. In the ischemic group, hypotensive shock appeared to be an invariable precipitating feature, being either directly observed or presumed from the history of onset. The most notable clinical feature was severe oliguria persisting for 1 or 2 weeks, occasionally longer. In approximately 75% of the patients, the daily urine output was 200 mg. or less, but in the remainder the daily output was somewhat greater, occasionally up to 600 mg. a day in the oliguric phase. The next characteristic feature was azotemia of progressive severity, with early and persistent gastrointestinal manifestations and usually late cerebral manifestations. Cerebral disturbance was worse in overhydrated patients. In approximately 50% of patients a mild hypertension with a mild or moderate tachycardia developed, and in 2 ventricular tachycardia developed.

Overhydration was probably present in all cases, but often it did not become manifest until restoration of the dry state in the phase of diuresis. Fifty per cent of the patients exhibited clinical evidence of overhydration, such as pulmonary edema and/or peripheral edema. Overhydration probably contributed to the symptomatic disturbance in all cases, but a definite correlation could be established

only in relation to the cerebral symptoms. Overhydration was entirely due to errors of clinical management. Anemia was more severe and was observed more frequently in the ischemic group, probably because of blood loss or acute hemolysis. However, other factors contribute to the anemia of both groups. Apart from hyperkalemia, electrolyte disturbance was relatively mild and only occasionally moderately severe, and hyponatremia and a reduction in plasma bicarbonate and chloride sometimes occurred. Hyperkalemia of moderate severity occurred in a number of the patients, being worse in those severely injured, but was a major cause of death in only 1. Electrocardiographic abnormalities correlated poorly with the hyperkalemia. During the phase of diuresis, electrolyte abnormalities became adjusted without specific therapy in most instances. Serious electrolyte depletion during this phase was uncommon, and it appears that severely injured tubules may retain or promptly regain the capacity to conserve electrolytes. Functional recovery, featured by a rapidly expanding diuresis, usually began in the second week with a rapid remission in symptoms, gastrointestinal disturbance being relatively persistent. The diuretic phase lasted for approximately a week and was followed by a rapid recovery in the renal mechanism for controlling water balance. The azotemia became worse in the first few days of the diuresis until excretory function became effective. Concentrating power was recovered slowly over a period of months. The mortality rate was 50%, and was worse in the ischemic than in the nephrotoxic group.

Two Years' Experience of Prednisone in Rheumatoid Arthritis. G. R. Fearnley, G. V. Balmforth and R. Blatchley. Brit. M. J. 2:1263-1266 (Nov. 30) 1957 [London].

The authors report on 167 patients with rheumatoid arthritis who were treated with various drugs for 2 years. Initially, 129 were given aspirin, 15 phenylbutazone, 8 cortisone, and 15 prednisone. Prednisone was given in a dose of 15 mg. daily. By the end of the 2-year period, 47 patients were receiving prednisone, 16 having been transferred to prednisone from aspirin, 8 from phenylbutazone, and 8 from cortisone. The increase from 15 to 47 patients treated with prednisone was accounted for by the failure of the other drugs. Thirty-seven of the 47 patients reported marked improvement, 6 reported only moderate improvement, 2 did not report any improvement, and 2 in their own estimation reported deterioration. Subjective improvement thus was reported by 90% of the patients treated with prednisone. The functional status was improved in 25 patients (about 50%). Dyspepsia was the commonest complication of prednisone therapy; it occurred in 11 patients, 2 of whom had peptic ulcers.

Thus, prednisone proved to be an effective antirheumatic agent in patients with rheumatoid arthritis whose response to other drugs was unsatisfactory. The effect of prednisone was better than that of cortisone. The improvement of some of the patients consisted not so much in doing more than they did previously as in doing what they always had to do more quickly, more comfortably, and more expeditiously. Prednisone produced substantial relief in a high proportion of patients. Relief was believed to be satisfactorily maintained in most of the patients, but it must be admitted that this belief depended in part on the personal reports of the patients which may be subject to many fallacies. The benefit obtained outweighed the risks and complications. The treatment with prednisone is justified in the cases of the wage-earner at the point of incapacity, the housewife unable to look after a young family, and the patient whose condition is deteriorating rapidly despite all other measures.

Hirsutism. W. H. Perloff, H. E. Hadd, B. J. Channick and J. H. Nodine. A. M. A. Arch. Int. Med. 100:981-985 (Dec.) 1957 [Chicago].

Hirsutism, excessive facial and/or body hair, represents a serious aesthetic and psychological problem to the woman so afflicted. Usually benign, it may be the sole manifestation of a serious endocrine disorder. Pituitary tumors are found occasionally in women with signs of virilization which include hirsutism; in most instances manifest adrenocortical hyperplasia is present, suggesting mediation through the adrenals. Hyperplasia or tumor of the adrenal cortex leads to 1 or a variable combination of 2 syndromes. If the abnormality involves only hydrocortisone metabolic pathways, Cushing's syndrome results, and when testosterone-like hormones are produced in excess the adrenogenital syndrome ensues. Pathological states or tumors of the ovaries, adrenal rests, Leydig-cell tumors, teratomata, and arrhenoblastoma are implicated in the pathogenesis of hirsutism. Diffuse luteinization (hyperthecosis) and polycystic ovaries of the Stein-Leventhal type are also etiological possibilities. In these 2 conditions, total neutral urinary 17-ketosteroids are normal or slightly to moderately elevated and diagnosis often depends on surgical exploration and histological examination of ovarian sections. Hirsutism has been reported in patients with thymic tumors and metabolic craniopathies (Stewart-Morgagni-Morel syndrome) and during menopause and pregnancy. Some women have congenitally sensitive hair follicles, and normal concentrations of serum androgens result in profuse hair growth. Most patients require careful study, including an extensive endocrine survey, before a diagnosis can be established.

When a functioning tumor of the ovary or adrenal gland is discovered, removal results in cure. More commonly, no definite etiology is found, and

the diagnosis of "idiopathic hirsutism" is made. This type of hirsutism is often familial, occurring in women whose ancestors stem from the Mediterranean area. Recent workers have indicated that idiopathic hirsutism is due to selective adrenocortical hyperfunction with disproportionate increase in the production of certain hormones. The authors were able to confirm these findings and apparently relieved both the metabolic abnormalities and the hirsutism with small doses of prednisone. Five women with the Stein-Leventhal syndrome and 16 in whom this and other causes of hirsutism had been eliminated were studied, photographed, and given 7.5-15 mg. of prednisone a day. Urinary levels of total neutral 17-ketosteroids, as well as $C_{19}O_2$ (strong androgens) and $C_{19}O_3$ (weak androgens) fractions, were measured in these patients. Total 17-ketosteroids and $C_{19}O_3$ fractions were generally higher in patients with hirsutism, but there was considerable overlapping with normal persons. The $C_{19}O_2$-17-ketosteroid fraction was uniformly elevated, and daily doses of 7.5-15 mg. of prednisone reduced these levels to normal or almost normal. Reduction in the amount, rate of growth, and coarseness of superfluous hair followed prednisone administration, particularly when wax depilation was performed concurrently. Improvement in both the hormonal excretory pattern and hirsutism persisted for at least 8 months after cessation of therapy. No important side-effects occurred, but one-half of all patients complained of transient fatigue. On the basis of this and other studies the authors believe that, despite the prevalence of idiopathic hirsutism and its familial distribution, it represents a type of adrenocortical hyperfunction which is abnormal, undesirable, and remediable.

Intestinal Polyposis Associated with Mucocutaneous Melanin Pigmentation (Peutz-Jeghers Syndrome). L. G. Bartholomew, D. C. Dahlin and J. M. Waugh. Proc. Staff Meet. Mayo Clin. **32**:675-680 (Nov. 27) 1957 [Rochester, Minn.].

This paper reviews 75 cases of Peutz-Jeghers syndrome, 68 of which have been reported in the literature and 7 of which are new cases reported from the Mayo Clinic. The chief stigma of this syndrome is the mucocutaneous areas of pigmentation. The pigment was found on the lips of all but 1 and on the buccal mucosa of all but 6 of the 75 patients. The areas of pigmentation may be oval, round, or irregular, and the color varies from brown or black to bluish gray. The pigmentation is found less frequently around the other facial orifices and on the extremities. The second and probably the most significant part of this syndrome is the presence of gastrointestinal polyps, and the third feature concerns the possible hereditary or familial nature of the disease. The accepted form of treatment for these polyps has been surgical removal. In the cases in which intussusception occurs, surgical treatment will continue to be necessary. The fear that the polyps are the forerunners of malignant transformation has, in the past, seemed to justify radical resection. From the evidence currently available, the intestinal polyps of this syndrome may be developmental anomalies similar in nature to hamartomas. More extensive pathological studies will be needed to help settle this problem.

Long-Term Tracheostomy in Extensive Bilateral Bronchiectasis. R. H. Overholt and M. S. Segal. New England J. Med. **257**:1108-1111 (Dec. 5) 1957 [Boston].

The authors are concerned with the use of long-term tracheostomy to facilitate intrabronchial aspiration in nonsurgical, suppurative bronchiectasis. In the 7 patients presented, intensive medical management had included the use of intermittent positive-pressure breathing, bronchoscopic aspirations, detergolytic aerosols, postural drainage, expectorants, liquefactants, antimicrobial agents, and steroids. The patients presented the appearance of chronic, progressive cardiopulmonary failure and debility. This followed in the wake of chronic bronchitis and bronchiectasis with associated ineffective cough mechanisms, retained bronchial secretions, and repeated bouts of penumonitis. Patients soon learn how to aspirate each side of the main bronchial system and to clean the tube. They are provided with catheters, connecting tubes, a trap bottle, and a suction attachment for a home water faucet. Each patient understands that the tube is inserted on a trial basis. If benefits do not outweigh the inconvenience, the tube can be withdrawn and the opening permitted to close. The decision about permanency of the tracheostomy is left with the patient. So far, all in this series have elected to continue to maintain this aid of self-aspiration of the airways.

Personality Variations in Bronchial Asthma: A Study of Forty Patients: Notes on the Relationship of Psychosis and the Problem of Measuring Maturity. P. H. Knapp and S. J. Nemetz. Psychosom. Med. **19**:443-465 (Nov.-Dec.) 1957 [New York].

The authors made psychodynamic studies on 40 patients with active, chronic, perennial bronchial asthma. Simultaneous study of pulmonary function showed a wide variation in physical manifestations, a feature characteristic of bronchial asthma. There was an equally wide variation in personality disturbance. All of the patients had emotional problems, which either were obvious to the examiner or were admitted by the patients, but there was no single personality "type." Seven transient, psychotic-like episodes occurred, 6 of them accompanied by an increase in asthma. Cortisone, though

given to more than half the group, did not provoke such reactions. There was no simple reciprocal relationship between asthma and psychosis. The patients appeared to range from mildly neurotic individuals, who had mild physical incapacity, to severely disturbed persons, who had drastic and crippling respiratory illness. To confirm this observation, the over-all maturity of the subjects was gauged on a roughly quantitative scale by 2 psychiatrists and was compared with independent assessments by 2 internists of the severity of pulmonary disease. There was a high correlation: the more severe the pulmonary disturbance, the more severe the personality disturbance, which had often existed for many years before the development of asthma. There was no patient with asthma of severe degree who did not also have major personality problems. The reverse does not appear to be true. Asthma seems one among many ways in which emotional difficulties manifest themselves.

Influenza with Involvement of Peripheral Nerves. F. Schwind and H. Solcher. München. med. Wchnschr. 99:1822-1823 (Nov. 29) 1957 (In German) [Munich, Germany].

The histories of several patients who had a peculiar clinical picture are presented. The first patient reported on had suddenly experienced pains on the right side of the neck and piercing pains in the chest on the same side while breathing and flaccid paralysis of the arm, paresthesias, and cough. The nerve plexus supplying the pulmonary apex, pleura, and scapular musculature was involved. The etiology could not be established. The second patient had a bilateral plexus neuritis. This patient, like the first, was subjected to various serologic tests, which were negative; however, in this patient complement fixation tests for A and B influenza virus were added, and these proved strongly positive. These tests for influenza virus were positive also in the 3rd and 4th patients presented, and it is therefore assumed that the peripheral motor and sensory disturbances represent a hitherto little-known clinical picture of infection with influenza virus.

C-Reactive Protein (CRP) in the Tuberculous Disease. L. Lenzini and G. Signorini. Sett. med. 45:411-422 (Aug. 15) 1957 (In Italian) [Florence, Italy].

Presence of C-reactive protein (CRP) in human blood is an index to the acute phase of inflammation within the body. The authors report experience with CRP in 150 hospitalized patients with tuberculosis. Primary phase of the disease was present in 21 patients, 6-14 years of age, the late primary phase (pleurisy with effusion) in 30, postprimary phase (exudative, productive, nodular, and fibrous types) in 39, and progressive phase in 60. Patients with primary complex were observed during retrogression or stabilization phases. C-reactive protein was not found in the serum of patients who were known to have had tuberculosis longer than 3 months. A slight positive reaction, (1-2 mm.) was present in those who were clinically ill less than 3 months. A positive reaction, varying from 2 to 8 mm., was obtained with serum of 26 patients (90%) who had pleurisy with effusion caused by M. tuberculosis. C-reactive protein was present in the serum of 29 patients with postprimary phase of tuberculosis. The value of the precipitation varied between 2 and 7 mm. Patients with the progressive form of tuberculosis were divided in 2 equal groups as to reactivated and chronic phase of the disease. These patients had been affected by tuberculosis for more than 2 years and had received antibiotic but not hormonal therapy. C-reactive protein was found in the serum of 24 patients (83.3%) with the reactivated progressive phase of the disease, and the precipitations varied from 2 to 7 mm. A negative reaction was obtained with serum of 27 patients (90%) with the chronic phase of tuberculosis. The authors conclude that the C-reactive protein test is probably a reliable index in distinguishing the active from the stabilized form of tuberculosis.

Course and Symptomatology of "Asiatic Influenza": Observation During an Epidemic in Barracks. R. Richterich. Schweiz med. Wchnschr. 87:1474-1476 (Nov. 30) 1957 (In German) [Basel, Switzerland].

Asian influenza, a variant of the A-virus influenza, first appeared in China in February, 1957, and reached Switzerland in August. Except for small outbreaks in schools, Asian influenza at first did not progress in an epidemic manner. In September an outbreak occurred in a school for recruits; this barracks epidemic attacked all except 80 of 440 recruits. The rapid progression is indicated by the fact that within 4 days 180 soldiers became ill with influenza. The symptoms and the course of the disease were quite characteristic and differed in certain respects from ordinary influenza. An incubation period of 12 hours to 3 days is followed by a viremic phase, during which the patient's temperature may go up to 40.4 C (104.7 F), and generalized lymphadenopathy and serous tonsillitis develop. In the second stage symptoms of the respiratory tract are most prominent, such as rhinitis, sinusitis, laryngitis, tracheitis, and bronchitis. Only a few complications were observed, such as purulent tonsillitis, fever, convulsions, and pancreatitis. Therapy was only symptomatic and in about a third of the patients unnecessary.

The author feels that from observations on soldiers it is difficult to draw conclusions regarding the course of Asian influenza among the civilian

population, because the soldiers are healthy young men in good physical training. It was found that Asian influenza was a benign although rather unpleasant disease. Serious complications were rare; neither bronchopneumonia nor encephalitis occurred. The authors regard as the greatest danger the rapid increase and decrease in fever, which in old and physically weakened persons might involve the danger of circulatory insufficiency. For this reason antipyretic drugs should be given only with great caution and in small doses. The surprising connection between the degree of fatigue and the severity of the influenza demands that physical exertion be reduced to a minimum during the epidemic. This was the only prophylactic measure which seemed to be of any value in the epidemic observed by the author.

Observations on Changes in the Mucous Membrane in Influenza. O. F. Ehm. München med. Wchnschr. 99:1904-1905 (Dec. 13) 1957 (In German) [Munich, Germany].

The author points out that T. Yung Tsü of Formosa, in August, 1957, called attention to so-called "influenza spots." He observed in many influenza patients small dots, yellowish-white in color, on the oral mucosa, chiefly around the excretory duct of the parotid gland and opposite the molars. The number of dots varied from 3 to more than 10. They are quite distinct from Koplik's spots. Hemorrhagic dots were observed on the palate of 1 patient. There are reports stating that similar enanthems were observed in earlier influenza epidemics. Since the diagnosis of influenza may be difficult, particularly in sporadic cases, a specific enanthem would be a great aid. The author watched for dots on the oral mucosa in 211 patients during the present influenza epidemic caused by the A-virus. He found that 34.5% of the patients had the dots observed by Yung Tsü, but a much larger number (58%) had petechial hemorrhages in the mucous membranes, which in almost half of the patients were situated in the papilla of the parotid duct. These alterations were still manifest 3-4 weeks after the influenza had abated.

Epidemiologic and Clinical Considerations on 457 Cases of Epidemic Hepatitis As Observed in a Military Environment in Morocco. H. Garnung, J.-A. Colson, R. Hugonot and others. Press. méd. 65:1969-1971 (Nov. 30) 1957 (In French) [Paris].

The authors report on 457 men with epidemic hepatitis among the French troops in Morocco, 266 of whom were treated at a military hospital in Casablanca between October and December, 1956, and 191 of whom were treated at a military hospital in Fez between August, 1956, and January, 1957. The epidemic attacked many persons, but most of the cases were benign. Only 1 of the 266 patients and none of the 191 patients died. Early symptoms consisted of fever up to 40 C (104 F) in 18% of the patients and up to 38 C (100.4 F) in 31%, nausea, vomiting, diarrhea, or constipation in 47%, and enlargement of the spleen in 3%. These general and functional signs frequently preceded the appearance of jaundice by 3-4 days. Headache occurred in 76% of the patients and cutaneous manifestations, such as urticaria or pruritus, in 20%. Jaundice was mild in most patients, with a bilirubinemia varying between 50 and 70 mg. per 100 cc. according to Van den Bergh's technique. The liver was enlarged in only 20% of the patients. As a rule the icterus subsided within 8 to 10 days. Duration of hospitalization on the average was 26 days. Complete recovery without any sequels occurred within 30 to 45 days in most of the patients. Recurrence of jaundice was observed in 8 patients and prolonged jaundice for more than 2 months in 3 patients. Temporary albuminuria occurred in 50% of the patients and temporary glycosuria in 2. Meningoencephalitis associated with facial paralysis and paralysis of the trigeminal nerve occurred in 1 patient. These data show that even in the course of benign epidemics exceptional cases with neurological complications and rare fatal cases similar to those of acute yellow atrophy may occur.

Treatment of Polycythemia Vera with Radioactive Phosphorus. I. I. Cowan. Wisconsin M. J. 56:501-505 (Dec.) 1957 [Madison].

Polycythemia may be either primary or secondary. The primary type is characterized by a high red blood cell count, an increase in the red blood cell volume, and an enlarged spleen. An adequate history and a complete physical examination with a careful evaluation of the red blood cell mass by total blood volume determinations will establish the diagnosis. The leukocyte count may be high. Late in the course of the disease a true leukemoid reaction may occur, and it may be difficult to differentiate this reaction from a true leukemia. Hemorrhages are a frequent accompaniment of leukemia, while thrombosis is usually seen in polycythemia. The severe secondary type of polycythemia is caused by congenital heart disease or pulmonary disease. Other secondary polycythemias occur in the presence of chronic cardiac or pulmonary disease. Radiophosphorus should not be used in the treatment of the secondary type of polycythemia.

The treatment of polycythemia vera is concerned with the reduction of the mass of circulating red blood cells to a level approaching normal. Radioactive phosphorus has been used in the treatment of polycythemia vera for the past 8 years in the Isotope Department of Marquette Medical School. Observations are presented on 38 patients treated in this manner since 1948. All were treated on an

outpatient basis. The therapeutic doses were administered with use of all necessary precautions. With administration of the phosphorus intravenously only a small percentage is lost or excreted in the urine and stools. There is no danger, as far as the patient's contact with other members of his family is concerned, because of the short beta radiation emitted. The method proved satisfactory. It is a simple and easily administered form of therapy. It does not produce symptoms of radiation sickness or local or systemic reactions. It produces longer and more complete remissions than other forms of treatment. In almost one-half of the patients the administration of 2 to 5 doses resulted in remissions lasting from 18 to 24 months. Using the proper precautionary measures, such as the divided dose method, it is less hazardous than some of the other methods of treatment. A late complication of the disease may be leukemia, which also occurs in patients not treated with radioactive phosphorus. The etiologic relationship between this therapy and leukemia is not established but remains a possibility. Life expectancy is better than in patients with treated pernicious anemia or treated diabetes mellitus.

Raynaud's Disease Among Women and Girls. R. W. Gifford Jr. and E. A. Hines Jr. Circulation 16:1012-1021 (Dec.) 1957 [New York].

From 1920 to 1945 Raynaud's disease or Raynaud's phenomenon was diagnosed in 756 female patients at the Mayo Clinic. Data gleaned from a review of the clinical records and from follow-up questionnaires constitute the basis for the present report. Raynaud's phenomenon may be defined as "an episode of contraction of the small arteries or arterioles of the extremities resulting in intermittent changes in color of the skin of the extremities, such as pallor, cyanosis, or both." Raynaud's phenomenon is a symptom. When it is primary, that is, when it exists in the absence of conditions or diseases to which it may be secondary, it is properly called "Raynaud's disease." Allen and Brown elaborated on Raynaud's original criteria for a diagnosis of Raynaud's disease. Their criteria are (1) episodes of Raynaud's phenomenon excited by cold or emotion; (2) bilaterality of Raynaud's phenomenon; (3) absence of gangrene, or, if present, its limitation to minimal grades of cutaneous gangrene; (4) absence of any other primary disease that may be causal, such as occlusive arterial disease, cervical rib, or organic disease of the nervous system; and (5) symptoms for at least 2 years.

When the diagnoses of the 756 women were revised according to the criteria of Allen and Brown, the original diagnosis of Raynaud's disease was considered incorrect for 127 patients and questionable for 252. Follow-up information from 208 of the 252 patients with a questionable diagnosis revealed that 52.9% did have Raynaud's disease. In 13.5%, diseases with which Raynaud's phenomenon is commonly associated (rheumatoid arthritis, acrosclerosis, and dermatomyositis) developed. The Raynaud phenomenon subsequently disappeared in 13.9% and remained unilateral in 1.9%. The remaining 17.8% of the patients were dead. Six patients were known or were presumed to have died of disseminated lupus erythematosus with which Raynaud's phenomenon is commonly associated. Although the causes of death were not known for 19 patients, the young age at which many of them died suggests that their Raynaud's phenomenon may have been secondary to a serious disease. The authors found that validation by the criteria of Allen and Brown assure a 95% accuracy in diagnosis.

Review of the records of 474 women and girls who had Raynaud's disease and follow-up information obtained from 307 who were treated conservatively confirms the benign nature of this disease. It caused no deaths and very little disability. Amputations of terminal phalanges for complications of Raynaud's disease were necessary in 0.4% of the patients before coming to the clinic and for none during the follow-up period. Raynaud's phenomenon became less troublesome or disappeared in 46%. Trophic lesions of the fingers and sclerodactylia improved or disappeared in the majority of women who had these complications. No major amputations were necessary, and gangrene did not occur. Raynaud's phenomenon can be a manifestation of many conditions and diseases of which Raynaud's disease is the most common and least serious.

Overweight and Hypertension. T. Bjerkedal. Acta med. scandinav. 159:13-26 (No. 1) 1957 (In English) [Stockholm].

The author reports on 14,784 adult persons who were employed in 112 industrial plants in Norway and whose records made by plant physicians contained complete information as to sex, age, body weight, height, and systolic and diastolic blood pressure given in millimeters of mercury. There were 11,063 men and 3,721 women. The data of these persons showed that the average systolic and diastolic blood pressure rises with increasing relative body weight in all age groups. By comparing the frequency distributions of the systolic and diastolic blood pressure values in groups of persons underweight, normal weight, and overweight of the same age, it was found that with increasing weight the distribution curves of blood pressure values shift slightly to the right without essential alteration of the shape of the curves. This seems to indicate that the main influence of obesity on the blood pressure is a small increase in the systolic and the diastolic blood pressure values in all per-

sons, since there is no distinct accumulation of persons with very high blood pressure values among the obese.

This small increase in blood pressure value is believed to depend on the effect of the circumference of the upper arm on the auscultatory blood pressure readings. The increase in blood pressure averaged from 1 to 2 mm. Hg between 2 consecutive 5% weight groups. These findings are in agreement with what might be anticipated in the light of Ragan and Bordley's measurements of blood pressure by the direct (intra-arterial) and the indirect (auscultatory) method which disclosed the too-high auscultatory measurements in persons with large arms. This small increase in the measured blood pressure in obese persons may explain why in some earlier studies a higher incidence of persons with hypertension were found in this group, when the upper limit of normal blood pressure was placed at 140/90 mm. Hg. Contrary to the common assumption that there is a higher incidence of persons with hypertension among those who are overweight, the conclusion drawn from this study is that there is no relationship between obesity and hypertension.

SURGERY

An Evaluation of Biopsy–Frozen Section of the Ampullary Region and Pancreas: A Report of 68 Consecutive Patients. H. J. Spjut and A. J. Ramos. Ann. Surg. 146:923-930 (Dec.) 1957 [Philadelphia].

Biopsies, on which a frozen section was done at the time of abdominal exploration of 68 patients, were evaluated in determining the nature of lesions of the ampullary region and pancreas. Of the 68 patients, 49 had a neoplasm and 19 had a nonneoplastic disease. The neoplasms included 39 carcinomas and 3 islet cell adenomas of the pancreas, 6 carcinomas of the ampulla of Vater, and 1 carcinoma of the common duct. The nonneoplastic lesions consisted of chronic inflammation and fibrosis of the pancreas, pseudocysts of the pancreas, 2 abscesses of the body of the pancreas, and 1 benign proliferative lesion of the ampullary epithelium. An erroneous diagnosis was made with the aid of the frozen-section process in 6 of the 68 patients; the immediate accuracy of the frozen-section process thus was about 91%. All of the errors occurred in the cancer group and in each instance represented an underdiagnosis of the lesion. One case counted as an error was thought to be cancer but could not be definitely diagnosed as such. No benign lesions were diagnosed as malignant. Three of the 68 patients had complications attributable to biopsy. Two of the complications were pancreatic abscesses and 1 a fistula. These appeared 30, 8, and 14 days after the biopsy respectively. Two patients in whom complication occurred did not have neoplasms; the third had carcinoma of the head of the pancreas.

Three of the errors were made in the face of extensive fibrosis and chronic inflammation associated with carcinoma of the pancreas. One error was made on a carcinoma with abundant mucin production; no carcinoma could be seen with the frozen section but was readily apparent with the permanent section. The 5th error was made in the failure to recognize an islet cell adenoma from the body of the pancreas. Fibrosis, chronic inflammation, fat necrosis, duct proliferation, accessory pancreatic ducts, and epithelial proliferation contribute to the difficulty of pancreatic biopsy but do not detract from its value. Of importance in the evaluation of pancreatic biopsy is the follow-up information on the 19 patients with a diagnosis of "no cancer"; 3 of the 19 patients were subsequently shown to have carcinoma. Biopsy with frozen section of the pancreas and ampullary region is considered to be an accurate, informative, and reasonably safe procedure.

Indications for Surgical Intervention in Patients with Combined Aortic and Mitral Stenosis. C. d'Allaines and T. Herrero. Presse méd. 65:1795-1797 (Nov. 6) 1957 (In French) [Paris].

The authors report on 10 patients with combined aortic and mitral stenosis who were operated on. Six patients had purely mitral symptoms, 2 had predominantly mitral symptoms associated with occasional painful attacks of retrosternal constriction, and 2 had predominantly aortic symptoms with dyspnea on exertion. An extensive anterolateral left thoracotomy was performed in the 4th intercostal space. Mitral valvulotomy was performed through the left atrium either with the finger or with the dilator; aortic valvulotomy was performed with the aid of a valvotome or more often with an aortic dilator with 2 blades. There was only 1 operative death, which occurred in a patient with 2 myocardial infarcts, total arrhythmia, and intra-atrial thrombosis; the patient died of acute cardiac failure 4 hours after the operation. The 9 patients who survived were followed up for periods of 6 months to 2½ years. Late results were satisfactory and definitely better than in patients who were operated on for aortic stenosis alone. Function was improved, pulmonary edema disappeared, dyspnea on exertion was less pronounced, and anginal attacks no longer occurred. A systolic aortic murmur often persisted.

Combined simultaneous valvulotomy is justified in the presence of combined aortic and mitral stenosis. With the aid of pressure studies one may decide which of the 2 valvulotomies should be performed first. If the aortic stenosis is of a severe degree, aortic valvulotomy should be performed first; if not, one should begin with mitral valvulotomy, and the operation should be continued with

aortic valvulotomy only if the transaortic gradient measured on the operating table reaches 50 mm. Hg. Under such conditions the combined operation is warranted, although "blind" valvulotomy for aortic stenosis without opening up the aorta may be of relative efficacy. The operative risk is not increased and the result is not compromised.

Carcinoma of the Thyroid: Incidence in Surgically Removed Nodular Thyroid Gland. P. T. McGannon and F. F. Allbritten Jr. J. Kansas M. Soc. 58:809-813 (Dec.) 1957 [Topeka].

This is a review of experience with a referred hospital population of 171 patients with nodular goiters which were surgically removed. Twenty-three of 171 patients having single or multiple nodules in the thyroid gland had malignant lesions, an incidence of 13.4%. Fourteen patients in the group of 23 with malignant lesions did not have clinical evidence of malignant disease, an incidence of unsuspected cancer of 8.6% in the entire group of patients with solitary or multiple nodules in the thyroid gland. Cancer was found in 8 of 19 male patients, an incidence of 42%. The incidence of carcinoma in 152 female patients with nodular goiter was 9.2%. Carcinoma was present in 16.6% of patients with solitary nodules and in 10.7% of those with multinodular glands. This difference is not so great as that indicated in other reports.

Duration, size, and symptoms of lesions in no way separated benign from malignant lesions. Six of 19 patients with carcinoma are alive 5-15 years after surgery, a 5-year survival rate of 31.6%. It is concluded that the incidence of carcinoma in nodular lesions of the thyroid is sufficiently high, in comparison with the existing mortality rates, that all nodules of the thyroid gland should be removed.

Occult Lymphatic Metastases in Malignant Melanoma of the Skin. R. E. Johnson. Ann. Surg. 146: 931-936 (Dec.) 1957 [Philadelphia].

Of 106 patients with malignant melanoma of the skin who were admitted to the Ellis Fischel Cancer Hospital in Columbia, Mo., between 1940 and 1954, the primary lesion was controlled by the initial complete excision in 65. In an attempt to obtain specific information as to the frequency and the location of occult lymphatic metastases, 2 approaches were used. Waiting and seeing what turns up in the form of regional lymph node metastases or of satellite nodules in the lymphatic plexus intervening between the primary site and the nodes was practiced in 33 patients. The regional nodes were removed by a prophylactic resection for histological study in 32 patients and in 3 of the 32 the regional nodes, and the intervening lymphatic plexus were removed by an "en bloc" resection. The first metastases to become manifest in the group of 33 patients who did not undergo prophylactic resection were in the regional nodes in 7 patients, and satellite nodules in the intervening lymphatic plexus were observed in 4 patients. Four of the 32 patients who underwent prophylactic resection had occult metastases in the nodes, and 6 had satellite nodules appearing in the intervening plexus. Thus, 21 of the 65 patients (about 33%), had occult metastases at the time of treatment of the primary tumor. The site of the primary lesion was the head and neck in 34 patients, the trunk in 11, the upper extremity in 4, and the lower extremity in 16. The incidence of occult lymphatic metastases ranged from 1 in 5 (7 of the 34 patients with the primary lesion in the head and neck) to 1 in 2 (12 of the 27 patients with the primary lesion in the trunk and lower extremity), depending on the anatomic site of the tumor. Five of the 21 patients were alive and free from the disease for more than 5 years and 1 was alive with cancer for more than 5 years, giving a 5-year survival rate of at least 29%. No reasonable means of increasing this figure by extended surgical treatment is apparent. No clear-cut case for or against prophylactic resection of lymph nodes can be made.

Gastroduodenal Hemorrhagic Diathesis: A Report of Ten Cases Treated by Vagectomy. G. Mixter Jr. and J. W. Hinton. New York J. Med. 57:3808-3814 (Dec. 1) 1957 [New York].

The authors review the results obtained in the management of massive upper gastrointestinal hemorrhage on the Fourth Surgical wards at the Bellevue Hospital in New York in the past 28 years. Since 1928, when they began keeping special records on this type of case, various forms of treatment have been used. The 403 patients reviewed all had peptic ulceration; patients with hemorrhage from esophageal varices, carcinoma, or leiomyoma were omitted. Many of the data summarized here have been presented previously, but a survey over the whole period reveals trends in treatment from completely conservative, with a mortality rate of 12%, to extensively surgical treatment with the mortality rate reaching intolerable levels. At the time surgical mortality rose to levels above 40%, it was evident that residents, whose experience with the problem was limited, should not be required to take too great a share of the responsibility. The mortality figures reflect not only the medical care but also the character of the patient load. The authors believe that their current mortality figures are acceptable for the indigent, poorly nourished, and often neglected patients who constitute the bulk of their ward population.

During recent years the indications for surgical interference during medical care of hemorrhage from peptic ulceration have become better defined. The wise surgeon refrains from surgery in such circumstances unless there is good evidence for

frank ulcer. In the latter case, particularly if the patient is over the age of 45, the necessity of controlling a major vessel in the base of a callous ulcer far outweighs other risks. However, there are some patients who, after resection or at autopsy, are found to have gastritis or shallow, small ulcers of esophagus, stomach, or duodenum. There are even those who become exsanguinated, and yet no source of hemorrhage can be identified. The authors cite reports which indicate that, in 12 of 25 patients requiring emergency operation for uncontrolled gastrointestional hemorrhage, no ulcer could be identified. These observations demonstrate the impossibility of separating the patient with truly surgical bleeding with an open vessel in a chronic ulcer from the patient with diffuse bleeding whose superficial ulcerations do not involve the larger vessels. The 10 patients whose histories are presented were from this "cryptogenic" group. They were treated by subdiaphragmatic vagus resection only, and this had a beneficial effect on the hemorrhagic diathesis. The avoidance of incision or resection of stomach or intestine should decrease both mortality and morbidity. Bilateral vagus section, if effective in halting the hemorrhage, would be preferable to the currently recommended gastrotomies and gastrectomies.

Left Heart Catheterization by the Transbronchial Route: Technic and Applications in Physiologic and Diagnostic Investigations. A. G. Morrow, E. Braunwald, J. A. Haller Jr. and E. H. Sharp. Circulation 16:1033-1039 (Dec.) 1957 [New York].

The authors describe the technique and instrumentation of catheterization on the left side of the heart by the transbronchial route and state that more than 500 such catheterizations have been performed at the National Heart Institute without mortality or serious morbidity. Perhaps the most essential requirement for successful transbronchial left heart catheterization is the participation of an experienced bronchoscopist. Good topical anesthesia and a smooth introduction of the instrument are mandatory. The procedure has been carried out even in severely ill patients when careful attention has been directed to their general preparation and the timing and dosage of preanesthetic drugs. The presence of severe tachycardia or frequent ventricular extrasystoles has usually constituted a contraindication to the procedure. The method lends itself well to serial studies in the same patient. Numerous patients have had catheterization 3 or more times, and 1 individual has had 7 transbronchial catheterizations of the left side of the heart. The procedure has been found useful in a variety of clinical investigations and in the preoperative selection and postoperative assessment of patients with valvular heart disease.

Operative Risks Associated with Surgical Methods of Removal of Colon and Rectum: Review of 516 Cases. R. Mosimann. Helvet. chir. acta 24:503-515 (Nov.) 1957 (In French) [Basel, Switzerland].

The authors report on 516 patients who underwent resection of the colon and rectum between 1938 and 1956. One hundred of the 516 patients died, 145 had local complications, such as suppuration of the surrounding tissues, fecal fistula, and ileus, and 109 had thromboembolic accidents and bronchopneumonia. Of the 516 patients 110 were subjected to a hemicolectomy of the ascending colon, 131 to segmental resection of the descending colon, 203 to abdominoperineal resection of the rectum, and 72 to several other methods of resection of the colon and rectum. Since the number of patients in the last group is too small for evaluation, only the results obtained in the 444 patients in the first 3 groups are discussed. One hundred ninety-nine of the 444 patients were operated on between 1938 and 1948, and 245 were operated on between 1949 and 1956; all the operations were performed in 1 stage. There were 43 operative deaths among the 199 patients, a mortality rate of 21.6%, and there were 43 deaths among the 245 patients, a mortality rate of 17.5%. Since the mortality rate for patients with hemicolectomy of the ascending colon before 1949 was 20%, as compared to 18% after 1949, and that of abdominoperineal resection of the colon 23% before 1949 and 22.3% after 1949 while the mortality rate of segmental resection of the colon was 20% before 1949 and 11% after 1949, the prognosis of only this last method of resection has become definitely more favorable.

Although the reduction in the mortality rate in the course of the last 8 years was not as great as one would have expected, it was notable and may be attributed to the preoperative disinfection of the intestine which resulted in an impressively diminished incidence of peritonitis and temporary fecal fistula. General complications, such as bronchopneumonia, thrombosis, and embolism, showed an increase in incidence of 20 to 30% during the period between 1949 and 1956. There were 16 deaths resulting from peritonitis among the 199 patients operated on between 1938 and 1948, as compared to 3 among the 245 patients operated on between 1949 and 1956. There were 5 deaths resulting from thrombosis or embolism during the first period and 13 during the second period. Although there is no definite answer to the question of whether the generalized use of antibiotics and blood transfusion might have been responsible for the increased incidence of thrombosis and embolism, the striking correlation between the increase in the incidence of these complications and the wider use of these methods of treatment makes it advisable to use the latter only in cases in which they are indispensable.

Diverticulum of the Pericardium with Observations on Mode of Development. H. C. Maier. Circulation 16:1040-1045 (Dec.) 1957 [New York].

A diverticulum of the pericardium may develop secondary to cardiac disease and pericardial effusion. When discovered on roentgenographic examination, the appearance may simulate cardiac or aortic aneurysm, vascular anomalies, cardiac and pericardial tumors, and mediastinal cysts. The author presents evidence concerning the mechanism of development of a diverticulum of the pericardium on the basis of 2 personally observed cases, some autopsy observations, and an analysis of cases recorded in the literature. The development of a large diverticulum that was not roentgenographically demonstrable until some years after an attack of idiopathic pericarditis is recorded. Although congenital factors may play a predisposing role by providing a weak area in the parietal pericardium, an increase in intrapericardial pressure with pericardial effusion seems to be the important causative factor in many cases. A pericardial diverticulum usually results from the gradual stretching of a herniating portion of the inner serous layer of the parietal pericardium that bulges through the split or weakened outer fibrous layer of pericardium. Evidence supporting the concept that pleuropericardial cysts and a pericardial diverticulum may have a common origin is indicated by a case in which both lesions were associated. Congenital diverticulum of the pericardium seems to be extremely rare.

Reoperations in Tight Mitral Stenosis: The Problem of Recurrence of Stenosis. P. Soulié, F. Joly, J. Carlotti and M. Servelle. Presse méd. 65:1987-1990 (Dec. 4) 1957 (In French) [Paris].

The problem of reoperation for a commissurotomy is discussed on the basis of 17 cases. In 8 of the patients reoperation was necessary because of failure of the commissurotomy. Diverse causes were responsible. During the early era of use of commissurotomy it occasionally proved impossible to rupture the commissures of very narrow orifices with the finger. These were generally not the calcified but the fibrous valves. In 3 of the 8 commissurotomy failures dilation with the finger was not possible. The presence of an organized auricular thrombosis, however, was the most frequent cause, being responsible for 5 of the 8 failures.

Recurrence of the mitral obstacle was responsible for reoperation in 9 of the 17 patients. The incidence of this recurrence varies in different reports —from 22 in 1,000 to none in 600 commissurotomies. The 9 cases reviewed here were observed in 400 commissurotomies, of which the first 180 were performed with the finger, whereas 95% of the remaining number were instrumental. The 9 patients who had recurrences all had been operated on during the early period. Recurrence of the stenosis seems to be most frequent in young subjects, 6 of the 9 in this group being less than 30 years old. A clinical and hemodynamic syndrome of the recurrence of the stenosis should be recognized. It is characterized by a development in 2 stages. It often poses difficult diagnostic problems, requiring differentiation from other conditions likely to compromise the future of the patient operated on for mitral stenosis.

The mitral stenosis recurs by a new welding of the commissures or by a valvular repair, apparently associated either with the further evolution of the rheumatic process or with a nonspecific sclerocicatricial process. However, the primary condition that permits secondary occlusion of the mitral orifice is the inadequate commissurotomy. This study provided definite evidence of the superiority of instrumental commissurotomy and of the value of systematic postoperative treatment with anticoagulant and anti-inflammatory substances for long periods.

Thoracoabdominal Aneurysm Involving Celiac, Superior Mesenteric and Renal Arteries: Report of a Case Successfully Treated by Resection and Nylon-Graft Replacement. J. H. Davis, J. W. Benson and R. C. Miller. A. M. A. Arch. Surg. 75:871-879 (Dec.) 1957 [Chicago].

Aneurysm of the thoracoabdominal aorta involving the celiac, superior mesenteric, and both renal arteries is a relatively uncommon entity. A survey of the literature revealed only 5 patients who have undergone successful resection of aneurysm of this extent. The present case is believed to be the 6th documented instance of a patient surviving such a procedure and the first in which a nylon-graft replacement has been used. A 41-year-old Negro man was admitted with the chief complaint of severe lumbar back pain which was constant, throbbing, and of sudden onset during a bowel movement. There were recurrent episodes of backache of moderate severity which were exaggerated by physical activity during the 6 weeks prior to admission. Examination revealed a well-developed, well-nourished man, in moderate distress from severe lumbar pain, with a blood pressure of 170/90 mm. Hg, pulse rate of 80 per minute, temperature 36 C (96.8 F), and respiration rate 20 per minute. The heart was not enlarged, there was a regular sinus rhythm, and no murmurs were heard. The chest was clear to percussion and auscultation and the movements of the diaphragm were normal. There was some spasm of the abdominal musculature and moderately severe guarding bilaterally. There were hypoactive bowel sounds, a mass palpable in the left epigastrium, which appeared to be pulsating, and an estimated 50% reduction in

the volume of the right femoral pulse. A systolic murmur was heard over both femoral arteries and in the midline of the abdomen. The peripheral pulse was decreased in the right leg as compared to the left leg.

On exploration a large aneurysm was found involving the thoracoabdominal aorta (both dissecting and penetrating the wall of the aorta), the celiac, the superior mesenteric, and both renal arteries. A prosthesis was manufactured from a woven nylon aortic graft, onto which were sutured stubs of frozen-dried iliac arteries to provide the celiac, superior mesenteric, and both renal arteries. The aneurysm was then resected, the graft inserted, and the blood flow reestablished. The insertion of a by-pass, as advocated by DeBakey, was accomplished. The insult to the kidneys from prolonged ischemia was reflected in a moderately severe anuria which required 7 days for return to normal volume. Approximately 20 days lapsed before the blood urea nitrogen returned to normal. It would appear from this instance and from reports by other investigators that good recovery may occur after renal artery occlusion of at least 1 and perhaps 2 hours. The effects of ischemia on the intestine are difficult to evaluate. Once bowel function returned, it appeared to be normal and there was no evidence of gastrointestinal hemorrhage or mucosal slough in the stools. Likewise, the effects of ischemia on the liver are difficult to evaluate, although a cephalin-flocculation test of 2+ in the immediate postoperative period is in keeping with the studies of Child and others on total hepatic artery ligation in the monkey, in which the cephalin-flocculation test rose to 1+ or 2+. This increase was the only abnormal finding. Some oxygenation of the liver probably occurred from portal blood flow on restoration of blood flow through the aorta, since the inferior mesenteric artery was intact.

Considerations Regarding "Recurrence" of Bronchial Carcinoma. G. Maggi. Chir. torac. 10:331-346 (Aug.) 1957 (In Italian) [Rome, Italy].

Reports of recurrent surgical interventions for bronchial carcinoma in patients who had been subjected to a pneumonectomy or a lobectomy are infrequent in the literature. The author reports on a male patient, 58 years old, who was operated on for a suppurating cancer of the lower lobe of the left lung in 1952. Symptoms started 1½ years before the operation. At operation a large peripheral squamous tumor was removed. There was no evidence of blood-borne or lymphatic vessel metastasis. The surrounding parenchyma was free from metastatic areas and from carcinoma in situ. A large hilar lymph node with a chronic lymphnoditis was not involved. Two and a half years later, the patient complained of the same symptoms that preceded the first operation. On the 2nd operation, a squamous tumor from the upper left lobe was removed. The histological diagnosis was bronchial carcinoma. The lymph nodes at the bifurcation of the bronchi were invaded. The patient was still living and well a year after the second operation. The opinion of the author is that the second neoplastic lesion was not a metastatic but a new primary cancer, because it developed from the bronchial epithelium.

The Postoperative Radical-Mastectomy Syndrome: Its Treatment with Stellate Ganglion Block. D. C. Moore, L. D. Bridenbaugh, J. W. Baker and C. S. Stone. A. M. A. Arch. Surg. 75:946-951 (Dec.) 1957 [Chicago].

The postoperative radical-mastectomy syndrome is caused by the extensive surgery necessary to cure a malignant invasion of the breast. The characteristic sign of this syndrome is edema of the arm and the presence of one or more of the following symptoms: accumulation of fluid under the skin flaps and in the axilla, delayed wound healing, pain in the arm and/or the chest, lymphangitis, induration of the arm and/or the chest wall, limitation of motion of the shoulder girdle, and hypertrophic cicatrix formation. The following factors, any of which either singly or in combination is capable of causing vasospasm, have been cited as the cause of the edema of the arm and could be responsible for the other signs and symptoms of the syndrome: (1) venous obstruction, (2) lymphatic-vessel destruction, (3) infection, (4) mechanical obstruction of the vessels by scar formation and metastatic tumors and/or fat fold, (5) irradiation therapy, (6) skin grafting, and (7) removal of the axillary vein during operation. Chronic vasospasm regardless of its cause tends to perpetuate itself and often becomes worse, setting up a "vicious cycle," and can, in many instances, be the sole cause of the postoperative radical-mastectomy syndrome.

The efficacy of stellate ganglion block in correcting chronic vascular spasm and thereby reducing the edema of the arm after radical mastectomy has been shown by Hanelin and others, who report persistent subjective improvement in 20 of 25 cases of edema of the arm. One hundred patients, ranging in age from 35 to 78 years, whose signs and symptoms had been present from 1 week to 5 years after surgery received 2-12 stellate ganglion blocks. Sixty-three of the patients showed marked improvement, 21 showed moderate improvement, and 16 of the patients showed no improvement. In the latter group only 9 of the 16 patients submitted to the prescribed series of blocks, i. e., approximately 10 blocks. Inasmuch as chronic vascospasm is believed to be the causative factor in the syndrome, failure to correct vascular spasm early may result in fibrosis or scarring sufficient to hold the blood vessels in a chronic state of diminished caliber. In

such instances the action of stellate ganglion block is three-fold. First, it tends to eliminate the vasospasm caused by surgery, infection, or accumulation of fluid which in turn probably reduces the attendant pain. Second, it increases the blood supply to the skin flap and chest wall after the blood vessels of the breast have been removed, which has the effect of softening the old scar or keeping the new scar supple and thus of preventing a slough of the skin flap and infection. Finally, any form of therapy is a good morale builder, particularly when improvement from it is noticeable to the patient. The results of a single block are seldom dramatic, and experience has led the authors to believe that, unless a patient is willing to submit to 7 to 10 blocks, stellate ganglion therapy should not be instituted. The refusals to continue the treatment after 4 or less blocks (as occurred in 7 of 100 patients) were due to the minor complications that may accompany the block procedure: (1) pain while the needle is being placed, (2) hoarseness, (3) Horners syndrome, and (4) paralysis of the arm. On the basis of this series it is felt that stellate ganglion block therapy should be instituted together with medical and surgical treatment for patients who exhibit the characteristic signs and symptoms of the postoperative radical-mastectomy syndrome.

Personal Experience from Gastrectomy for Hemorrhages of the Digestive Tract: Observations on 94 Cases. J. Patel and J. Lataste. Presse méd. 65:1811-1814 (Nov. 9) 1957 (In French) [Paris].

Ninety-four gastrectomies were performed in the service of one of the authors for severe recent hemorrhage of the digestive tract between 1950 and 1956. There were 14 deaths (14.91%). Three of the patients had only melena; 91 had hematemesis. Gastric ulcer caused hemorrhage relatively more often than did duodenal ulcer, although duodenal ulcer predominated among the patients with ulcers. This was particularly true of the severe and moderately severe hemorrhages. Hemorrhages caused by gastric cancers were rarely severe, so that surgery was rarely urgent in these patients. Surgical treatment is urgent in case of severe hemorrhage; the prognosis becomes more unfavorable if an expectant attitude is adopted in these patients. There were 84 subtotal gastrectomies with 8 deaths (9.5%), 5 total gastrectomies all followed by death, and 5 gastrectomies for exclusion with 1 death.

Gastrectomy for exclusion constituted an emergency operation in patients with a severely bleeding duodenal ulcer. When the hemorrhage is profuse, it may be necessary to extend the dissection, expose the choledochus, and, if necessary, drain it. Resection of ulcers at the anastomosis of previous gastrectomies did not prove dangerous; it proved successful in all 5 patients in whom it was carried out. The prognosis of total gastrectomy, however, is grave, particularly in debilitated patients. In such patients a partial gastrectomy (at the upper pole, if necessary) should be preferred, even in the presence of a carcinoma. The postoperative course in the 80 patients who recovered was uneventful, and the late results were as good as in patients with uncomplicated ulcers. Postoperative deaths were more frequent in alcoholics and in patients with bleeding gastric ulcers.

Hirschsprung's Disease: A Lethal Problem in Infancy. G. W. Dorman. A. M. A. Arch. Surg. 75:906-913 (Dec.) 1957 [Chicago].

Prior to 1954, Klein and Scarborough collected 50 cases of Hirschsprung's disease in newborn infants and reported 70% fatalities. English literature since 1947 lists 156 proved cases in infants under 6 months of age, of whom 76 (48.7%) died. The type and severity of symptoms are governed by a combination of circumstances affected by the degree of compensatory hypertrophy and dilatation of the proximal intestine which is capable of peristalsis, the degree of inspissation and impaction of feces within the proximal and distal segments, and the degree of obstruction imposed by the aperistaltic intestine. The most frequent manifestation of Hirschsprung's disease in a newborn child is acute intestinal obstruction with gaseous abdominal distention, hyperactive peristalsis, meconium or fecal vomiting, and scanty or absent passage of meconium stools during the first few days of life. Less commonly, a profuse and malodorous water diarrhea may dominate the picture. In children past the neonatal age the symptoms of chronic constipation, abdominal enlargement, and diminishing incidence of vomiting gradually replace the more dramatic symptoms of acute intestinal obstruction observed in younger infants.

Of the 11 infants treated by enterostomy, 10 have improved dramatically and have done well to date. Six have later undergone definitive resection of the aganglionic intestine with restoration of continuity by the Swenson procedure. This operation should not be attempted in small infants, since later closure of the enterostomy and definitive resection are best done when the child has reached about 20 lb. (9072 Gm.) body weight and is in good general health. Bodian, Carter, and Ward summarized the literature prior to 1951 and pointed out the familial incidence of this disease, estimating a 20% probability with variation according to sex and previous incidence within the same generation. They also estimated that about 90% of such patients have only the rectum and rectosigmoid colon affected, while in the remaining 10% a longer segment or possibly an entire aganglionic intestine will be affected. A few rare instances of alternating segments of aganglionic and normal intestine have

been reported, but in the overwhelming majority of patients no normal intestine exists between the most proximal beginning of the aganglionic lesion and the anus. A myenteric anomaly extending proximally into the ileum presents a picture similar to that of meconium ileus complicating cystic fibrosis of the pancreas. Creation of a proximal enterostomy is recommended for all afflicted infants under 6 months of age in order to avoid impending serious complications and to improve on the appalling mortality incidence.

Treatment of Severe Hæmorrhage. P. Firt and L. Hejhal. Lancet 2:1132-1137 (Dec. 7) 1957 [London].

In some patients with severe hemorrhage the quantity of blood theoretically required for replacement does not accord with the ability of the cardiovascular system to accept intravenous transfusion without overloading. The authors investigated this question in a series of experiments. One group of experiments demonstrated that the cause of cardiac overloading and failure during rapid intravenous transfusion is not, as has been assumed, solely the amount and rapidity of blood inflow. Another group of experiments (in which citrated instead of heparinized blood was used) suggested that the cause of cardiac overloading and failure is citrate, added to prevent coagulation. It was found that citrate, even in small doses, produces vasoconstriction in the pulmonary vascular bed and in larger doses depresses myocardial activity, both effects leading to cardiac overloading and failure. Under conditions of shock, cardiac disease, severe anemia, and liver damage, small doses of citrate may be dangerous—even those contained in a slow transfusion of small quantities of blood. Blood without citrate can be safely transfused at rates many times greater than can citrated blood, not only intravenously but also intra-arterially. The advantage of intra-arterial transfusion in the treatment of shock and hemorrhage lies only in the increased rate of citrate filtration into the interstitial fluid, compared with the rate in intravenous transfusion, thus lowering the citrate concentration reaching the myocardium and pulmonary vascular circuit.

The author shows further that the effect of citrate during transfusion can be counteracted by calcium gluconate and that this effect can be potentiated by the intravenous administration of procaine. The use of calcium for the treatment of citrate intoxication is well known; the authors have merely applied this to transfusion techniques. A method of rapid intravenous transfusion with simultaneous administration of calcium and procaine was critically evaluated in a selected group of surgical, obstetric, and gynecological patients, and the results confirmed the experimental data.

Problem of Preservation of Ampulla of the Rectum in Surgical Therapy of Nonspecific Ulcerative Colitis. F. Baldrati. Clinica 17:323-339 (No. 5) 1957 (In Italian) [Bologna, Italy].

The author describes surgical management of nonspecific ulcerative colitis in 4 patients, between the ages of 31 and 40 years, aiming at preserving the continuity of the intestine. Surgical therapy included preservation of the ampulla of the rectum, colectomy, which was followed by anastomosis between the descending colon and the rectum in 1 patient and ileoproctostomy in 3. The hospitalization period ran from 17 to 30 days. No postoperative complications caused by surgical intervention were observed. Patients had a liquid stool during the first few days after operation, which improved later and stabilized at 4 to 5 solid stools a day. The 1st patient, who was subjected to colectomy combined with anastomosis, was seen 7 years after the operation. She had resumed her household duties, had regained weight, and had normal solid stools 2-3 times a day. The 2nd patient had been frequently seen for 3 years. He was able to return to hard work as agricultural technician and had gained 15 kg. in weight. He passed 4-5 semi-solid or liquid but never bloody stools a day. Recently he was hospitalized for an abscess adjacent to the anus, which was successfully treated. The 3rd patient was last seen 15 months after the operation. She was able to resume normal life, gained 12 kg., and passed 4-5 semi-solid stools a day. The 4th patient, who was seen 8 months after operation, had a similar recovery. The ampulla of the rectum of the 4th patient was normal, but the termination of the ileum was larger and occasionally subject to spasmodic attacks.

The Results of Thrombophlebitis Treatment. V. I. Popov and P. P. Alekseev. Vestnik Khir. 79:23-31 (Nov.) 1957 (In Russian) [Leningrad].

The authors advocate early ambulation, leg and feet exercises, and, in some cases, internal administration of anticoagulants as basic prophylactic measures against postoperative occurrence of thrombophlebitis and phlebothrombosis. They stress the advantages in the prophylaxis of these complications of the performance of intravenous infusions in the distal direction, that is, against the blood current. When the great saphenous vein is used for a prolonged transfusion with either blood or various solutions in the course of major surgical interventions, the needle should be directed distal to the current of the blood. The frequent occurrence of thrombophlebitis and phlebothrombosis of the great saphenous vein after prolonged infusions is due to the effect of the infused substances on the vessel wall because of their insufficient dilution by the recipient's blood. The effect is one of vasospasm,

interference with the nutrition of the vessel, desquamation of the endothelium of the intima, and the formation of intraluminal thrombosis. Of 295 patients operated on and treated by intravenous transfusion given in the proximal direction of the blood current, 47 (16%) developed thrombophlebitis, while of 106 patients in whom intravenous transfusions were performed in the distal direction thrombophlebitis occurred in 4 (3.7%).

For the actual treatment of acute or chronic thrombophlebitis, the authors advocate intra-arterial infusion of penicillin and novocaine into the artery of the affected limb. The effect of novocaine on the peripheral nervous system is to eliminate pathological reflexes and thus to prevent vasospasm, while penicillin, in addition to its antiseptic property, increases the permeability of the tissues and stimulates the function of the reticuloendothelial system. The treatment consists of daily intra-arterial infusion of 20 cc. of 0.5% novocaine solution and of 250,000 to 300,000 units of penicillin for 10 to 14 days. Daily estimation of prothrombin and coagulation time of blood are performed. Anticoagulants are given if the blood prothrombin rises. Of 54 patients treated for acute or chronic thrombophlebitis by this method, 39 have given an excellent result and the rest a satisfactory result.

NEUROLOGY & PSYCHIATRY

The Role Played by the Destruction of the Globus Pallidus in the Improvement of Parkinson's Syndrome. G. Guiot. Semaine hôp. Paris 33:3711-3714 (Nov. 6) 1957 (In French) [Paris].

The results obtained by the author with surgical destruction of the globus pallidus, which was performed on patients with Parkinsonism, agree with those obtained by other workers in that they warrant the use of this surgical method from the practical point of view because of the definite improvement of symptoms. However, it is difficult to conceive of this method physiologically. It is much more difficult to control the tremor than to suppress hypertonia and to improve akinesia. The most simple effect of pallidotomy is one of reduction of muscle rigidity. Although Bucy believes that the control of the tremor cannot be achieved without a lesion of the internal capsule, which is associated with the destruction of the globus pallidus, the author obtained highly satisfactory results concerning tremor as well as rigidity in 1 patient whose internal capsule had remained unimpaired. The tremor persisted in another patient despite damage inflicted on the internal capsule. Although unobtrusive symptoms of a motor injury definitely occur after pallidotomy, this "pyramidal touch" cannot be considered responsible for the improvement in tonus and kinetics when this improvement differs considerably from the effects of authentic pyramidotomy, when there is pronounced disproportion between the importance of the improvement and the occasionally observed pyramidal signs, and when the improvement consists precisely in the restoration of what one still considers the function of the pyramidal tract.

Improvement of hypertonia and akinesia seems to be definitely related to the destruction of the globus pallidus, while that of the tremor is still debatable. The exact anatomic definition of the effectively produced lesion and the critera for its effectiveness, i. e., its topography, extent, and quality, have not yet been firmly established. One may, however, state that the effectively produced lesion is situated in an area which has been approximately limited and is likely the most suitable for a thorough intervention on the pathophysiological mechanism of Parkinsonism.

Treatment of Delirium Tremens. L.-M. Gunne. Nord. med. 57:703-706 (May 16) 1957 (In Swedish) [Stockholm].

From March, 1952, to February, 1955, 44 patients with severe delimium tremens were treated by active routine methods, including electroshock, high doses of cortisone, vitamins B and C and supportive liver therapy, and parenteral administration of hypertonic and isotonic fluids, with promazine and later chlorpromazine as sedatives. Seven patients died. From March, 1955, to October, 1956, the medical treatment was limited to vitamins B and C, with antibiotics as needed. Sometimes blood pressure stimulants and antiepileptics had to be applied. Intensified observation of the patients was stressed, with rapid correction of threatening symptoms. Fluids were given mostly by mouth. Mainly, conservative therapy and careful nursing gave better results than did the earlier more active therapy. The mortality in 100 consecutively treated cases was 2%.

Experimental Cerebral Infarction: The Effect of Dicumarol. W. A. Sibley, J. H. Morledge and L. W. Lapham. Am. J. M. Sc. 234:663-677 (Dec.) 1957 [Philadelphia].

The authors produced cerebral infarction in 36 dogs by the injection of homologous clot fragments into the carotid artery. Eighteen of the 36 dogs were given orally a single dose of bishydroxycoumarin (Dicumarol) in amounts varying from 150 mg. to 200 mg. or about 10 mg. per kilogram of body weight. The other 18 dogs did not receive anticoagulant therapy and served as controls. Moderately or severely hemorrhagic cerebral infarction was frequently compatible with survival and clinical improvement in the untreated animals; thus, of 11 untreated animals which survived the infarction,

8 had hemorrhagic cerebral infarcts. A clinical course of progressive improvement was fatally reversed as a result of hemorrhagic changes occurring in and about the cerebral lesions in 4 of 12 animals surviving cerebral infarction by more than 24 hours and treated with bishydroxycoumarin. Death occurred in 2 of these animals in association with prolongation of prothrombin time of a degree not unusual in clinical practice. With greater prolongation of prothrombin time death occurred in the 2 other animals as late as the 9th and 14th days after infarction. Five of 7 animals surviving cerebral infarction and treatment with bishydroxycoumarin had infarcts of the brain which were grossly of the anemic variety.

The results of these experiments indicate that administration of bishydroxycoumarin increases the hemorrhagic tendencies of experimentally produced embolic infarcts of the brain in dogs. These findings are interpreted as providing confirmatory evidence for the belief of many clinicians that anticoagulant drugs are contraindicated after recent embolic infarction of the brain in man. Caution is suggested in the use of anticoagulant agents in cases diagnosed clinically as cerebral thrombosis, because of difficulties in clinical distinction between thrombotic and embolic infarction of the brain.

Hemiballismus Secondary to Metastatic Carcinoma of the Gall Bladder. L. J. Lemmen, J. S. Davis and E. R. Fisher. Neurology 7:873-874 (Dec.) 1957 [Minneapolis].

Hemiballismus, a type of involuntary movement which may result from a lesion in the contralateral subthalamic nucleus or its anatomic connecting pathways, was observed by the authors in a patient who had gallbladder carcinoma with a metastatic tumor nodule in the region of the subthalamic nucleus. The patient was a 59-year-old man, who experienced involuntary movement of the right arm for 1 month. This developed suddenly while he was shoveling coal into a furnace. Slight uncontrolled activity in the right leg was noted by his wife during the week prior to hospital admission. When first examined the patient was oriented, cooperative, and without aphasia. Recurrent, gross, purposeless "throwing" motion of the right arm, shoulder, and hand accompanied by facial grimacing was evident. The patient could stop these activities voluntarily for only 30 seconds. These abnormal movements would begin in a similar length of time if the extremity was externally restrained. An occasional kicking motion occurred in the right leg. General physical examination disclosed no abnormalities. Laboratory studies, including urinalysis and a complete blood count, and a serologic test for syphilis were within normal limits.

Subsequently, the patient became confused, his speech became explosive, and he had outbursts of animal-like cries. The oral or intramuscular administration of Nembutal every 4 hours resulted in somnolence and almost complete cessation of the involuntary movements. Reserpine, chlorpromazine, and zoxazolamine had no effect on the involuntary movements. Eight days before death he experienced melena for a 48-hour period and 3 days later had coffee-ground emesis and became unresponsive. Involuntary movements of the right upper extremity persisted until shortly before death. Autopsy disclosed a polypoid adenocarcinoma of the fundus of the gallbladder. A similar neoplasm was found in periportal lymph nodes, liver, and brain. Hemiballismus resulting from metastatic neoplasms in the subthalamic region has been reported most frequently from a primary breast tumor. The case presented is of interest because the patient's initial complaints were due to central nervous system involvement.

GYNECOLOGY & OBSTETRICS

The Prognosis of Carcinoma of the Endometrium in Its Different Stages Treated by Surgery Combined with Postoperative Radiotherapy. L. Lindgren. Acta obst. et gynec. scandinav. 36:426-438 (No. 4) 1957 (In English) [Stockholm].

The author reports on 525 women with carcinoma of the endometrium treated by postoperative radiotherapy at the Radiumhemmet in Stockholm. The cases are analyzed with special reference to the degree of infiltration of the growth in the uterine wall. Four hundred eleven of the 525 patients were treated by primary surgery combined with postoperative radiotherapy, and 114 received postoperative radiotherapy for recurrent carcinoma of the endometrium after primary surgery. Of the 411 patients, 347 had carcinoma of the body of the uterus, 29 had carcinoma of the body of the uterus and endocervical carcinoma, and 35 had carcinoma of the uterus and the ovaries. The prognosis was better in patients with superficially infiltrative carcinoma. This type predominated in patients in whom the body of the uterus alone or possibly also the ovaries were involved. In patients with carcinoma of the body of the uterus and endocervical carcinoma, the incidence of the deeply infiltrating type was higher, suggesting that this latter type was generally in an advanced stage, even in its primary site, at the time of diagnosis. The reverse held true in patients with carcinoma of the uterus and the ovaries. This suggests that carcinoma of the body of the uterus can spread by way of the fallopian tubes at an early stage when infiltration is still superficial.

The patients were grouped according to Reuterwall's histological classification. Superficial infiltration was more common with highly differentiated adenocarcinoma. This finding assumes importance

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in relation to the choice of treatment. The prognosis was much more unfavorable in patients in whom complete removal of the growth proved impossible or in whom perforation of the uterus had occurred accidentally either at operation or at preoperative curettage. It appeared to be of no importance to the results whether supravaginal or total hysterectomy was performed, provided the cervix was not involved and postoperative radiotherapy was given to the cervix and the vagina. Supravaginal hysterectomy carries an unfavorable prognosis if the cervix is involved. No relationship was found between the radium doses which were used and the obtained results. The doses used for postoperative radium treatment of patients with carcinoma of the endometrium were small compared with those doses given in primary irradiation treatment of the condition. The survival rates, i. e., a relative 5-year survival rate of 93.5% and a corrected 5-year survival rate of 97.3%, of patients with a superficial degree of infiltration subjected to hysterectomy and removal of both adnexa were so high that it may reasonably be assumed that the treatment given was sufficient. In addition it appeared to lessen the risk of vaginal and cervical recurrence. The corrected 5-year survival rate among patients with deeply infiltrating carcinoma of the body of the uterus was only 67.6% (81.9% in those in whom both adnexa were removed). Every effort should therefore be made to improve the results in the latter cases. These data show clearly that postoperative irradiation cannot be adequately planned in patients with carcinoma of the endometrium unless the degree of infiltration is known. Histological determination of the degree of infiltration, therefore, is of major importance.

Constitutional Virilism. D. Ferriman, P. K. Thomas and A. W. Purdie. Brit. M. J. 2:1410-1412 (Dec. 14) 1957 [London].

In an attempt to assess the clinical significance of idiopathic hirsutism in women, the authors compared the association between hirsuties and body build and 17-ketosteroid excretion in 43 hirsute and 101 nonhirsute women between the ages of 18 and 44 years. The association generally believed to exist between hirsuties and oligomenorrhea was investigated in 53 hirsute patients and 296 nonhirsute patients. The sisters and mothers of 29 women below the age of the menopause with a major degree of hirsuties were studied so as to ascertain the familial incidence of the condition. Results revealed an association between hirsuties and 2 other masculine characteristics in women, namely, increased shoulder width and raised 17-ketosteroid excretion. There was also a significant correlation between hirsuties and oligomenorrhea. The term "constitutional virilism" is a convenient one to describe the composite syndrome. The condition appears to be genetically determined, and the results obtained suggest that the inheritance is multifactorial.

Treatment with Anticoagulants of Pregnant Women with Previous Severe Toxemia. J. Løvset, K. Knutsen and A. Jakobsen. Acta obst. et gynec. scandinav. 36:492-498 (No. 4) 1957 (In English) [Stockholm].

The authors report on 12 pregnant women between 20 and 40 years of age or more in whom 1 or more fetuses had died in the course of previous pregnancies complicated by severe toxemia. These women had lost a total of 16 infants during the period between the 28th and 40th week of their pregnancies. They were given prophylactic anticoagulant therapy from the 4th or 5th month of pregnancy in an attempt to reduce the tendency to placental infarction caused by toxemia and to prolong the intra-uterine life of the fetus. All 12 patients gave birth to infants who survived. The weight of the babies varied from 2.5 kg. (5 lb.) to 4 kg. (9 lb.) and that of the placentas from 400 to 770 Gm. Some of the patients had a slight rise in blood pressure and an occasional trace of albumin in the urine, but none of them had preeclampsia or eclampsia. No complications due to anticoagulant treatment were observed.

Sarcoidosis: The Effects of Pregnancy and of Subsequent ACTH and Corticoid Therapy on the Disease. W. A. Peters Jr. and W. Spaeth. North Carolina M. J. 18:548-552 (Dec.) 1957 [Winston-Salem].

Sarcoidosis is characterized by tubercle-like lesions composed of epithelioid and giant cells but manifesting little or no caseous necrosis. Any organ may be affected, but the process is more prone to involve lymphoid tissue. Lesions also commonly occur in the skin, bones of the hands and feet, lungs, eyes, parotid gland, spleen, and liver. The 27-year-old woman whose history is presented had pulmonary sarcoidosis. During the 5 years that she was under observation, full-term pregnancy and delivery occurred twice. Remission of sarcoidosis took place during the early weeks of the first pregnancy, and relapse was observed within 3 months post partum. Remission was again induced with corticotropin therapy. After a subsequent pregnancy, relapse of sarcoidosis occurred within 3 months post partum. Remission was again induced with adrenal cortical steroid therapy.

The literature presenting evidence for the production of corticotropin by the human placenta is reviewed. It is suggested that the remission of the disease observed during pregnancy was due to placental production of corticotropin. It is concluded from this study and a review of the literature that therapeutic abortion is not indicated if the disease is discovered early in pregnancy. In an addendum, the authors mention the report appear-

ing in THE JOURNAL (164:158 [May 11] 1957), in which 16 pregnancies in 10 patients with sarcoidosis also demonstrated the ameliorating effect of pregnancy on sarcoidosis. It has been suggested that improvement of sarcoidosis during pregnancy may be due to the increase in the production of corticoids by the adrenals during gestation.

Rare Feticide Accident: Electric Shock. E. M. Baldi. Obst. y ginec. latino-am. 15:363-364 (Sept.-Oct.) 1957 (In Spanish) [Buenos Aires].

Accidents caused by electric shock are frequent, but reports of these accidents in pregnant women are extremely rare. Two cases have been reported in the literature and another has been reviewed. In all 3 cases, as well as in the case reviewed in this report, the electric shock was caused by a current of 220 v. The first woman received the electric shock in the 7th month of pregnancy. She had no burns. Hydramnious developed. Spontaneous delivery of a living infant occurred at the 8th month of pregnancy. The infant had scars (already epitheliazed) on the ears, elbows, knees, and dorsum of the hands and feet. He died 3 days after birth. No disease (syphilis or other) which might have caused the scars was found at autopsy. The second woman was in the 3rd month of pregnancy when she suffered the shock and burns. A few hours later metrorrhagia appeared which could not be controlled by medical treatment. The product of conception was removed by surgical evacuation of the uterus. In the case reviewed the woman was in the 6th month of pregnancy when she suffered the electric shock. Spontaneous delivery of a dead, macerated fetus occurred 3 weeks after the accident. The subject of this report was a multiparous woman at the 8½ month of normal pregnancy when she received the electric shock. Immediately after the woman had recovered from shock she noticed that the fetal movements had stopped; this fact was confirmed by the gynecologist. Spontaneous delivery of a dead macerated fetus occurred 6 days after the accident. Examination of the fetus did not reveal any cause of the sudden death of the fetus other than the electric shock received by the mother.

PEDIATRICS

Studies on Cyclic Neutropenia; A Clinical and Experimental Investigation. A. R. Page and R. A. Good. A. M. A. J. Dis. Child. 94:623-661 (Dec.) 1957 [Chicago].

The authors collected from the world literature 23 cases of cyclic neutropenia, a rare disease characterized by the regular disappearance of neutrophils from the circulating blood at approximately 21-day intervals. In 10 female patients between the ages of 3 and 64 years and in 13 male patients between the ages of 2 and 77 years the neutropenic phase of the cycle was generally associated with clinical manifestations of fever, malaise, and the appearance of ulcers in the oral mucous membranes. Other symptoms, which were not common to all the patients, included intermittent arthralgia, abdominal pain, sore throat, lymphadenitis, headache, ischiorectal infections, mental depression, conjunctivitis, and cutaneous ulcers. The authors present a detailed report on a 15-year-old white girl with cyclic neutropenia in whom the diagnosis was made at the age of 11 years. She showed the characteristic symptoms of the disease.

An extensive search was made in an effort to determine the causative mechanism of the disease. Transfusion of the neutropenic patient's blood into a patient with myelogenous leukemia and infusion of large amounts of the patient's serum and blood obtained during the neutropenic phase into 1 child with leukemia, 2 normal children, and 1 child with mild leukocytosis did not produce fever, oral ulcers, skin ulcers, or leukopenia. Even though 3 different methods of demonstration were used, no leukoagglutinins could be found at any time during the cycles of neutropenia. These findings suggest that there is no immunological basis for the disease. A toxic factor which might injure the polymorphonuclear leukocytes, account for the "toxic" appearance of the cells which was observed, and result in the cyclic neutropenia was sought by studying the migration and phagocytic ability of these cells. No evidence of the appearance of a factor injurious or destructive of neutrophils was found in the peripheral blood at any time. Serial bone marrow specimens obtained during various neutropenic phases revealed cyclic fluctuations of the concentration of reticulum cells, myeloblasts, promyelocytes, neutrophilic myelocytes, and neutrophilic metamyelocytes. These observations indicated that the cyclic neutropenia is due to a cyclic arrest of production of the entire neutrophil series. Studies of the patient's growth and development, menstruation, and specific pituitary-adrenal-gonadal function did not reveal any evidence of a hormone factor responsible for this syndrome. Taking advantage of the cyclic fluctuation in the neutrophil count, an attempt was made to evaluate the role of the neutrophils in several biological processes. Findings suggested that neutrophils do not perform a function essential to the production of circulating antibodies, that the production of acute-phase serologic reactions do not depend on the presence of neutrophils, that endogenous pyrogen derived from polymorphonuclear leukocytes does not play an important role in the reaction produced by these toxins in man, that neutrophils are not essential to the development of a high degree of refractoriness to the toxic and pyrogenic effects of gram-negative bacterial endotoxins, and that the neutrophilic infiltration in

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some way conditions the lymphocytic invasion and consequent macrophage accumulation in acute inflammation.

Attempts at treatment included prophylactic and therapeutic administration of antibiotics, parenteral injection of normal leukocytes during the neutropenic phase of the cycle, a thorough trial of both corticotropin and cortisone in large doses, splenectomy, and micrococcic (staphylococcic) vaccine therapy. None of these measures resulted in significant alteration of the cyclic neutropenia.

Ebstein's Anomaly: Presentation of Ten Cases. F. E. Mayer, A. S. Nadas and P. A. Ongley. Circulation 16:1057-1069 (Dec.) 1957 [New York].

The authors present observations on 10 patients with Ebstein's anomaly who were observed at the Children's Medical Center in Boston and who ranged in age up to 25 years. There were 4 males and 6 females. Postmortem material was available in 4; cardiac catheterization had been performed in 4 and angiocardiography in 2. The findings in these 10 patients were correlated with those reported in the literature to emphasize certain clinical features that are of diagnostic value. The symptoms are usually mild, with cyanosis, dyspnea, fatigability, and, commonly, a history of bouts of palpitation. The physical findings are characterized by normal growth, frequent cyanosis, and infrequent clubbing, a quiet cardiac impulse and a systolic thrill between xiphoid and apex, a triple or quadruple rhythm, a second sound diminished at the pulmonary area, and a combination of systolic and diastolic murmurs maximal at the lower left sternal border or apex. Phonocardiographic studies confirm the presence of a triple or quadruple rhythm, show a delayed first sound of normal intensity, and demonstrate a systolic murmur of moderate intensity and medium frequency and a presystolic murmur at the lower left sternal border and apex. Less constant is a mid-diastolic murmur in this area.

The characteristic electrocardiogram has tall P waves, frequently prolonged atrioventricular conduction, considerable right bundle-branch block, and right ventricular potentials of low amplitude. Radiologic examination reveals marked cardiomegaly, a contour consistent with enlargement of the right side, a narrow base, diminished pulmonary vascular markings, and a poorly delineated pulmonary artery. Angiocardiography reveals a huge right atrial chamber with delayed emptying, poorly opacified pulmonary radicles, and frequent evidence of a right-to-left shunt. Cardiac catheterization demonstrates a large atrium, displacement of the tricuspid valve to the left, moderately elevated right atrial pressure, normal right ventricular systolic pressure, and absence of a significant gradient across the pulmonary valve. Peripheral arterial oxygen unsaturation is usual. The authors stress the importance of clinical recognition of this entity in view of the hazard involved in undertaking cardiac catheterization and surgical procedures in these patients.

Investigation of the Metabolic Effects of Metacortandracin and Metacortandralone in Healthy Children. W. Tangheroni and R. Bartalena. Minerva pediat. 9:888-893 (Sept. 8) 1957 (In Italian) [Turin, Italy].

Metabolic effects of prednisone (Metacortandracin) and prednisolone (Metacortandralone) were studied in 10 healthy children, 8 to 12 years of age, divided in 2 equal groups. Each group received a daily dose of 15 mg. of prednisone and prednisolone, respectively, for a period of 7 days. Determination of blood and urine sugar levels was carried out before and after the administration of the steroids. Blood glucose level tended to rise slightly and was higher in the group receiving prednisone, remaining, however, within its physiological values. Cholesterol concentration of the serum increased markedly and doubled in some of the children. Urinary nitrogen and total protein levels did not rise appreciably. Hematocrit concentration rose in both groups and was more pronounced in the children of the group receiving prednisone. Excretion of potassium increased in 7 children and was more clearly seen in those given prednisone. Slight decrease of the concentration of sodium and chloride in the blood was observed in both groups. Fall in the number of circulating eosinophils was more pronounced in the group given prednisone. Both drugs caused suppression of urinary 17-ketosteroids. Diuresis appeared in both groups at the end of the trial. The steroids caused no alteration of either arterial pressure or of electrocardiographic findings and led to no change in body weight.

The authors conclude that the most important metabolic effect of prednisone and of prednisolone, as opposed to that of cortisone, was their intense diuretic action and the increased excretion of chlorides and sodium ions in the urine.

Duplication of the Stomach: A Case Report. W. B. Kiesewetter. Ann. Surg. 146:990-993 (Dec.) 1957 [Philadelphia].

The author reports on a newborn Negro female infant in whom a freely movable, hard mass about the size of an orange was palpated in the left upper quadrant just under the abdominal wall. Repeated bouts of vomiting led to physical examination, followed by radiologic demonstration of a large oval shadow of water density occupying the left upper quadrant. The mass seemed to impinge on the greater curvature of the stomach and to displace the transverse colon downward. Exploratory laparotomy revealed a duplication of the stomach at-

tached to the middle portion of the greater curvature. It was possible to resect the mass with small sacrifice of the stomach, since its attachment to the stomach was along a narrow strip that extended about 8 cm. The specimen was 8 cm. by 4 cm., with an attachment to the stomach 1 cm. in width. There was a common wall between the stomach and the mass, revealed by microscopic section. The infant's postoperative course was uneventful. Follow-up examinations showed full and normal development in all respects.

The findings in this infant would fit Bremer's concept of duplication of the stomach. He believes that duplication of the stomach may well occur from an inpouching of the mucous membrane of the large lumen of the stomach and that the mucosa then becomes adherent along one line; the muscular coats in some fashion follow around the adherence of the mucosa, and 2 separate tubes develop, attached to each other by a common seromuscular wall. A total of 27 cases of duplication of the stomach have been recorded in the English literature through 1956; 15 of these occurred in the pediatric age group. The case of the successfully treated infant is the 16th reported on.

Thyroid Dysfunction in Goitrous Children: Radioiodine Studies and Plasma Chromatograph Analysis for Thyroid Hormone. R. H. Kunstadter, R. M. Kohlenbrener and L. Oliner. A. M. A. J. Dis. Child. 94:682-690 (Dec.) 1957 [Chicago].

The authors report on 3 boys between the ages of 6 and 9 years, 2 of whom were brothers and presented the clinical aspect of goiter and suggestive hypothyroidism, and the third of whom showed goiter, dwarfism, and several congenital defects. The laboratory results indicated thyroid hyperactivity in all 3 patients. It was only after plasma chromatographic studies were done that the nature of the defect was revealed, i. e., that of apparent failure of the thyroid to deshalogenate the hormone precursors, which were released into the plasma. Normally, the precursors are not found in the plasma. Despite the fact that thyroid hormone was found in the blood of these patients, it is logical to assume that it was present in insufficient amounts, since peripheral signs of hypothyroidism were present. Quantitative thyroxin determinations were not done. The observed high radioactive serum protein-bound iodine concentration and serum protein-bound iodine level can be explained on the basis of circulating plasma iodinated hormonal precursors in addition to triiodothyronine and thyroxin.

The suggestion of clinical hypothyroidism in the 2 brothers and the goiters of all 3 patients can be explained on the basis of probable insufficient circulating thyroid hormone, resulting in increased release of thyrotropin. From the study of these 3 patients, it is evident that persons with inborn errors of thyroid metabolism may or may not manifest the usual clinical features of hypothyroidism. Determination of serum protein-bound iodine level, radioactive iodine uptake, and radioactive protein-bound iodine concentration may be insufficient to clearly define the metabolic abnormality. Chromatographic analysis of circulating radioactive protein-bound iodine compounds is necessary to define the defect. It would be helpful to know the plasma thyroxin level in both normal children and children with thyroid dysfunction.

Kernicterus and Mental Deficiency. C. B. Courville. Bull. Los Angeles Neurol. Soc. 22:177-182 (Dec.) 1957 [Los Angeles].

Mental deficiency is one of the serious residuals not infrequently found in children who have survived more advanced states of neonatal jaundice (kernicterus). This condition varies in degree, but in individuals with crippling motor involvement, the intellectual defect is usually so marked as to be described as an amentia. The author describes his studies of the structural changes in the brain of a boy who had developed jaundice after birth and who survived to the age of 4 years. The boy had a mental defect along with an advanced degree of spastic paralysis. At autopsy only a mild degree of frontal cortical atrophy was noted. On microscopic examination, however, a marked widespread patchy loss of nerve cells was found in this region. Since this pattern of change is also that found in cases of cerebral anoxia, the question is raised as to whether the blood pigment in neonatal jaundice may somehow affect the cortical capillary system as well as the individual nerve cells of the cortex and corpus striatum. It is more likely that anemia in the infant, secondary to destruction of red blood cells, results in a form of anoxemia (anemic form) which is capable of producing the typical cell loss in the cortex.

UROLOGY

Prolonged Treatment of Urinary-Tract Infections with Sulfamethoxypyridazine. H. G. Grieble and G. G. Jackson. New England J. Med. 258:1-7 (Jan. 2) 1958 [Boston].

Many patients with chronic urinary-tract infections are refractory to treatment with the available antibacterial drugs. The recent introduction of a new sulfonamide, sulfamethoxypyridazine, provided a drug that seemed suitable for the trial of long-term chemotherapy. This paper deals with its antibacterial effect among patients with urinary-tract infections and includes observation of drug levels in patients with and without renal insufficiency. The bacteriological data were considered suitable

for evaluation of the effectiveness of the drug in 48 patients. The average duration of treatment with sulfamethoxypyridazine was 35½ days per patient. Three-fifths of the patients were treated for at least 3 weeks, a third for a minimum of 6 weeks, and 6 patients for 60 to 250 days. Except for a few patients who were given daily doses of 1 Gm. of sulfamethoxypyridazine, all patients received an initial loading dose of 2.5 Gm. followed by 0.5 Gm. per day. Children were given comparable doses calculated on a weight basis. Nine patients had 2 courses of therapy, and 2 received 4 courses.

Antibacterial concentrations of free sulfonamide were maintained in the serum and the urine. Adverse reactions were observed in 6.4% of the patients during the first course of treatment. A favorable clinical response was observed in 80% of the patients with acute infections and 24% with chronic infections. Bacteriological cure was achieved in 21% of the group. The antibacterial effect was comparable with the results achieved with standard doses of other sulfonamides. Escherichia coli was the organism most responsive, whereas the results with other species were, in general, poor. Susceptible bacterial strains were eradicated after one or two weeks of treatment, or not at all. The nature of the bacterial infection and the therapeutic results were significantly influenced by certain host factors. The low proportion of patients cured of urinary-tract infections is not unusual. Mixed bacterial cultures and superinfections during and immediately after treatment were the principal cause for the failure.

Concepts of Pyelonephritis: Experience with Renal Biopsies and Long-Term Clinical Observations. G. G. Jackson, K. P. Poirier and H. G. Grieble. Ann. Int. Med. 47:1165-1183 (Dec.) 1957 [Lancaster, Pa.].

In an analysis of 4,425 autopsies, the authors found the incidence of pyelonephritis to be 9%. The lesions were of major pathological importance in one-third of the cases, or in 3% of the autopsies. After most of the current antibiotics became available, the incidence was still 6.3%. In another survey of 71 patients with predominantly unilateral kidney disease, who underwent nephrectomy within the decade from 1945 to 1954, pyelonephritis was present as a significant lesion of the resected kidney in 57% of the cases. A third group of 50 patients, selected because of bacteriuria, with or without symptoms, were subjected to biopsy of a kidney specimen. Seventy-five per cent of these had pyelonephritis according to the biopsy. The data from this group of patients are presented. Clinically, the 50 patients are classified as follows: Group 1 included 4 patients with asymptomatic bacteriuria. Group 2a was composed of 7 patients with acute pyelonephritis, characterized by fever, flank tenderness, dysuria, and cloudy urine; some had had previous similar attacks, followed by clinical and bacteriological recovery. In group 2b were placed 11 patients who had chronic urinary symptoms and persistent infection with intermittent episodes of acute illness. Group 2c included 18 patients who had had occasional backache or dysuria but no history of acute pyelonephritis. Finally, 10 patients, in group 3, had shown systemic symptoms, with azotemia and/or hypertension but few or no urinary symptoms.

The symptoms of patients with pyelonephritis were not a reliable index of the severity, or even of the presence, of the disease. Acute clinical pyelonephritis was often associated with the finding of gram-negative bacteria in biopsy specimens. The biopsy findings in the acute stage suggested a diffuse exudative reaction in the tubular portion of the kidney, with minimal interstitial nephritis. Kidney function was not impaired. Chronic pyelonephritis was more closely related to the duration of the infection than to the severity of the symptoms. Lesions appeared to be diffusely scattered throughout the kidney. The biopsy specimens showed infiltration of the interstitial tissues and variable degrees of glomerular and vascular inflammation. In advanced lesions, different histological components predominated, which suggested vascular or tubular obstruction. Individuals varied in functional impairment. Diminished renal blood flow, with relative ischemia and a proportional decrease in glomerular and tubular function, was characteristic and paralleled the severity of the structural abnormality. Bacteria were recovered from the majority of pathological biopsy specimens, and gram-positive strains predominated. Pyelonephritis secondary to other renal diseases was frequently accompanied by hypertension or azotemia. Bacteriuria without appreciable pyelonephritis also was observed. The results of treatment were related to the histological and clinical observations.

OPHTHALMOLOGY

Experience of Treating Retinal Venous Occlusion With Anticoagulant and Antisclerosis Therapy. S. Vannas and H. Orma. A. M. A. Arch. Ophth. 58:812-828 (Dec.) 1957 [Chicago].

In a comparative study of the experience gained at the Ophthalmic Clinic of the University of Helsinki from 1951 to 1956, there were 75 patients with retinal venous occlusions, a total of 81 thromboses in 77 eyes. Only 8 of these patients failed to report for a follow-up. The probable etiology of the occlusion was traced as far as possible. General sclerotic manifestations either with or without arterial hypertension were diagnosed in 63% of the cases; sclerosis of the fundal veins of the fellow eye was diagnosed in 72%. Mild, moderate, or severe arterial hypertension was established in 71%. An inflammatory factor (usually sinusitis) was found

in 13% and simple glaucoma in 10%. Sclerosis thus seemed to have an important role in the pathogenesis of the occlusion. The following therapy was evolved: At first, intensive anticoagulant therapy of 10 days to 3 weeks was given preferably with heparin (in exceptional cases with bishydroxycoumarin [Dicumarol] or a corresponding drug). In addition, vasodilator drugs may be employed. Inflammatory etiological factors must also be treated. Then, in patients with sclerosis antisclerosis therapy—100 mg. of heparin sodium intravenously (or 200 mg. subcutaneously)—is given twice a week and 100 mg. of vitamin E by mouth 3 times a day. Depending on the patient's condition, the therapy is continued for months or years.

Anticoagulant therapy was given to 35 patients with a total of 37 cases of retinal venous occlusion and to the control group, with 36 cases. The results achieved were as follows (control group in parentheses): good in 59% (14%), fair in 20% (28%), poor in 13% (16%), and nil in 8% (42%). Uncontrolled glaucoma developed in 2 (5) cases. As regards complications, not very dangerous hemorrhages occurred during bishydroxycoumarin therapy in 5 cases, and during heparin therapy in 1 case. Two weeks to 6 months after termination of short-time anticoagulant therapy recurrent occlusion reappeared in 4 patients, and 1 of these also had cerebral thrombosis, but this was not fatal. In the control group there appeared occlusion of the fellow eye in 2 patients, and death with cerebral or coronary thrombosis occurred in 5 patients. These complications indicate that the state of these patients is perhaps more dangerous without anticoagulant therapy. Anticoagulant therapy considerably improves the prognosis for patients with central vein occlusion. Even short-term therapy may suffice in some cases, but experience speaks for the greater efficiency of long-term therapy, especially in elderly patients.

Ocular Manifestations of Sickle-Cell Disease. G. Goodman, L. von Sallmann and M. G. Holland. A. M. A. Arch. Ophth. 58:655-682 (Nov.) 1957 [Chicago].

The ocular changes in the 5 patients with sickle-cell disease presented in this study were predominantly vascular in nature, involving retina, optic disk, and conjunctiva. Hemoglobin electrophoresis demonstrated sickle-cell hemoglobin C disease in 4 of the patients and suggested sickle-cell hemoglobin D disease in another. Fundus changes included retinitis proliferans, aneurysmal vascular dilatations, arborizing vascular networks, focal constriction, dilatation, sheathing and obstruction of arterioles and venules, the development of chalk-white vessels due to changes in intravascular contents, preretinal hemorrhages which closely simulated retinal tears, and vitreous and retinal hemorrhages. Vascular changes were also noted on the optic disk and bulbar conjunctiva. Histological findings in 1 patient with sickle-cell retinopathy showed retinal and vitreous hemorrhage, retinal gliosis blending with a preretinal fibrous membrane, extensive new vessel formation, obliterated vessels, perivenous lymphocytic cuffing, and sickled cells intravascularly and in the areas of hemorrhage. The findings in these patients are discussed in relation to previous reports of sickle-cell retinopathy, the pathophysiology of sickle-cell disease in other organs, and the correlation of ocular pathology with the different genotypic forms of sickle-cell disease.

The following points are stressed: 1. Sickle-cell retinopathy may be manifest as an acute or chronic obstructive vascular disease, with vitreous hemorrhage as a frequent complication. The occurrence of such pathology in Negroes or in Caucasians of Mediterranean origin warrants testing for a sickling tendency and performance of hemoglobin electrophoretic studies if sickling is present. It is suggested that patients with Eale's disease (retinal periphlebitis associated with recurring vitreous hemorrhages) should be investigated for evidence of sickle-cell disease. 2. The major features of sickle-cell retinopathy can be accounted for on the basis of vascular stasis and obstruction involving both arterial and venous systems. This is the common pathological denominator of sickle-cell disease in the organs which it affects. 3. The small number of reported cases of sickle-cell retinopathy, as well as the inadequacies in either the ophthalmological or the hematological examination of these patients, makes it impossible to ascertain the incidence of retinopathy in the different types of sickle-cell disease. However, patients with sickle-cell hemoglobin C disease appear especially prone to ocular manifestations. Furthermore, sickle-cell trait may also lead to eye complications, as well as obstructive vascular episodes in other organs, and should no longer be considered a clinically benign carrier state. 4. Renal and ocular lesions are frequently associated in sickle-cell disease, as in other "small vessel" diseases, such as hypertension and diabetes.

THERAPEUTICS

Pyrazinamide and Pyrazinamide-Isoniazid in Pulmonary Tuberculosis: Comparison with Other Chemobiotic Combinations. G. Poggio and A. Wrubl. Minerva med. 48:2795-2804 (Sept. 1) 1957 (In Italian) [Turin, Italy].

The antituberculous activity of pyrazinamide in 34 patients with recent forms of pulmonary tuberculosis and the effect of the combined therapy pyrazinamide-isoniazid in 100 patients with recent and chronic forms of pulmonary tuberculosis were

studied. The chronic form of the disease was present in 50 patients of the second group who had been already given other antibiotics. The first group received pyrazinamide in daily doses of 3 Gm. for 2 months; the second group received the daily dose of 3 Gm. of pyrazinamide and 250 mg. of isoniazid for 3½ months. Symptomatic improvement, such as disappearance of fever, increase in weight, and restoration of sedimentation rates to normal, was observed in most patients of either group. The sputum became negative for Micrococcus tuberculosis in 60% of the patients in the first group and in 70% of the second group. Roentgenographic changes showed improvement in about 81% of the patients in both groups. Administration of pyrazinamide alone was particularly effective in patients with recent, not severe forms of the disease; its therapeutic action, however, weakened in 2 months. The effectiveness increased in intensity and duration when pyrazinamide was administered concurrently with isoniazid. Mild side-effects were observed in few patients and required only a temporary suspension of the chemotherapy. Marked therapeutic results were obtained in 10 patients of the first group and in 25 of the second group. Two patients showed a worsening status. The remaining patients either reached a state of clinical and roentgenologic stabilization or were transferred to other hospitals. The authors suggest that the antituberculous activity of pyrazinamide-isoniazid is superior to other antituberculous drugs.

Allergy to Chlorpromazine Manifested by Jaundice. L. E. Hollister. Am. J. Med. 23:870-879 (Dec.) 1957 [New York].

The author detected jaundice in 17 of 900 patients who were treated with chlorpromazine. All 17 patients were men between 24 and 75 years of age, 13 of whom received the drug for treatment of mental disorders, 3 for relief of pain and 1 to determine the effect of the drug on essential hyperlipoidemia. Only 2 of the 17 patients were known to have had definite liver disease before treatment with chlorpromazine was instituted. The clinical picture of fever, gastrointestinal symptoms, and malaise followed shortly by jaundice occurred within the first 4 or 5 weeks of treatment with chlorpromazine. The daily dose of the drug at the onset of jaundice varied between 100 and 400 mg. The jaundice was usually of mild degree, the highest level of serum bilirubin being 14.2 mg. per 100 cc. The highest elevations of alkaline phosphatase (27, 22, and 18 Bodansky units) were associated with serum bilirubin values of 2.4, 4.4, and 1.9 mg. per 100 cc. respectively. The highest levels of serum bilirubin (14.2 and 9.5 mg. per 100 cc.) were associated with rises in alkaline phosphatase activity to 12.4 and 9.8 Bodansky units respectively. Enlargement or tenderness of the liver and pruritus were occasionally noted. Cephalin flocculation tests yielded positive results in 16 patients, but the thymol flocculation test gave positive results in only 4. The positive results were usually transient. Adrenocortical hormones or antihistamines were given to 7 patients at the onset of jaundice. Eight patients did not receive any specific treatment, and 2 patients continued to receive either the same or an increased dose of chlorpromazine after the onset of jaundice. The effect of treatment was equivocal, but the use of adrenocortical hormones or histamines should be considered in severe cases. Continued treatment with chlorpromazine did appear to prolong the duration of jaundice, although both patients had metastatic carcinoma and were in poor general health.

If liver function tests indicate that the jaundice is of the obstructive type, a diagnosis of jaundice due to chlorpromazine therapy can almost certainly be made. Skin tests to demonstrate allergy to chlorpromazine were unrewarding. However, 9 of 11 patients with jaundice due to chlorpromazine therapy who were challenged with the drug from 10 days to 17 months after the initial episode of jaundice showed evidence of retained sensitivity. No cross-sensitivity with promazine could be demonstrated, suggesting that other phenothiazine derivatives might be substituted in treatment of patients in whom sensitivity to chlorpromazine develops. Prevention of this complication of chlorpromazine therapy is difficult, but prompt detection and withdrawal of the drug might make for a milder course. The risk of jaundice from chlorpromazine has been no deterrent to use of this drug when it is the drug of choice.

Pyrazinamide in the Treatment of Pulmonary Tuberculosis. F. Serafini, E. Fasano and T. Lubich. Riv. pat. e clin. tuberc. 30:198-202 (July-Aug.) 1957 (In Italian) [Bologna, Italy].

Sixty-four patients with postprimary pulmonary tuberculosis received pyrazinamide in daily doses of 2.5 to 3 Gm. for a period of 1 to 6 months. Twelve patients, divided in 2 equal groups, were given pyrazinamide for a period of 1 to 2 months. The first group had recent forms of tuberculosis and had not previously received antituberculous drugs. Pyrazinamide brought about improvement in the general condition of the patients, negative reaction of the sputum for mycobacterium tuberculosis in 2, and improvement in the roentgenologic findings in 2. Further treatment with streptomycin and isonicotinic acid hydrazide healed the ulcerations in the latter 2 patients. The second group had chronic types of tuberculosis and had previously received antituberculous chemotherapy. Pyrazinamide treatment led to a subjective relief of symptoms in 4 patients but without roentgenologic changes. The only improvements observed a month after with-

drawal of pyrazinamide were negative sputum in 1 patient and restoration of body temperature to normal in 2. Combined therapy of isonicotinic acid hydrazide and streptomycin, or isonicotinic acid hydrazide and *p*-aminosalicylic acid was reinstituted after withdrawal of pyrazinamide.

The remaining 52 patients with chronic tuberculosis, in some of whom collapse therapy failed, were given a combination of pyrazinamide and isonicotinic acid hydrazide. Subjective relief of symptoms was observed in about one-half of the patients, whereas roentgenologic changes and objective improvement occurred in only a few patients. Of 10 patients with fever, 5 became afebrile. Temperature rose in 1 patient in whom pyrazinamide therapy was discontinued. Slight gain in weight was noted in 15 patients, marked diminution of cough and sputum in 12, disappearance of sputum in 3, and reversal of sputum in 3. Roentgenologic changes were observed in 8 patients, consisting in improvement of exudation in 4, narrowing of cavities in 2, and disappearance of the ulcerative process in 2. The authors conclude that pyrazinamide alone is effective in the treatment of patients with recent types of tuberculosis, who have not previously received other antituberculous chemotherapy. Better results would be obtained with either streptomycin or isonicotinic acid hydrazide alone. Patients with old cavities, who had previously received other chemotherapy, and those in whom collapse therapy failed derived benefit from pyrazinamide treatment. No unfavorable hepatic, cardiac, or circulatory side-effects were observed.

Tuberculous Meningitis and Hydrocortisone Acetate Administered Locally: Changes of the High Protein Content in the Cerebrospinal Fluid. P. F. Peruzzi. Riv. clin. pediat. **60**:198-210 (Sept.) 1957 (In Italian) [Florence, Italy].

Increase of the protein content in the cerebrospinal fluid indicates the presence of an inflammatory reaction to the causative organism of tuberculous meningitis. The objective of the clinician is to institute a chemotherapy which will dissolve and eliminate the tuberculous exudate. The author reports on 11 patients, 3 to 43 years of age, with tuberculous meningitis and high protein content in the cerebrospinal fluid, who were admitted to the Pediatric Clinic in Florence in the period 1954 to 1956. Hydrocortisone acetate was given to them in daily doses of 5 to 7 mg. by intracisternal instillation and 1-2 mg. by lumbar route. Systemic and local antituberculous therapy was concomitantly maintained. Hydrocortisone acetate therapy produced a gradual improvement of the protein content in the cerebrospinal fluid in all patients but 1. Intracisternal instillation is the most effective route for administration of hydrocortisone acetate. Lumbar route is effective only in combination with intracisternal instillation. The effect of hydrocortisone acetate medication is two-fold: it arrests the process or eliminates formation of the granulating tissue, and it restores the capillary permeability. The author concludes that hydrocortisone acetate therapy is effective whenever there exists a possibility of the formation of a block.

Treatment of Experimental Histoplasmosis with Amphotericin B. G. L. Baum, J. Schwarz and C. J. K. Wang. A. M. A. Arch. Int. Med. **101**:84-86 (Jan.) 1958 [Chicago].

The authors studied amphotericin B (an antibiotic isolated from an unidentified species of Streptomyces) in 150 hamsters that had been experimentally infected with Histoplasma capsulatum. It was found that amphotericin B, either alone or in combination with sulfadiazine sodium, is an effective therapeutic agent in experimental histoplasmosis in hamsters. The addition of sulfadiazine sodium improves the effect of the treatment. The fact that the preparation is made less turbid by the addition may represent an increased amount of amphotericin B in actual solution or finer dispersal of the amphotericin B, if it is not actually solubilized. Therefore, sulfadiazine sodium may not add any fungistatic or fungicidal effect of its own but may act purely by making more of the amphotericin B available to act against H. capsulatum. The authors believe that, because of the apparent increased solubility of this particular preparation of amphotericin B and its low toxicity, it should be tried in human histoplasmosis. Since this disease is benign in the majority of patients and the clinical course is protean, care will have to be exercised in ascribing clinical effectiveness to this drug. There are infrequent cases of progressive disseminated disease which are commonly fatal, and in these this drug may prove to be the first effective treatment.

Radiculomyelopathy After Oral Mercurial Diuretics. S. C. Sommerfelt. Nord. med. **57**:852-854 (June 13) 1957 (In Norwegian) [Stockholm].

A patient with cardiac failure, treated with an orally administered mercurial diuretic (3-chloromercury-2-methoxypropylurea) for 9 months, developed severe symptoms of toxic lesion of the nervous system. Four weeks after withdrawal of the agent, the urinary excretion of mercury was approximately 400 mcg. daily, pointing to a marked mercury retention and possible mercurial poisoning. Urinary excretion of mercury continued for many days after the administration of a single dose of the compound, and daily dosage probably increased the tendency to mercury accumulation. Intermittent administration, as usually applied on

parenteral administration of mercurial diuretics, is recommended when mercurial diuretics are given orally, so that the body can eliminate at least most of the ingested mercury before each new dose. Attention must be paid to possible symptoms of mercurial intoxication, also from the nervous system, with immediate termination of the treatment if this should arise.

PATHOLOGY

New Formation of Vascular Wall on the Basis of Synthetic Arterial Prostheses. G. Petry and G. Heberer. Arch. klin. Chir. 286:249-290 (No. 3) 1957 (In German) [Berlin].

The authors report the results of animal experiments performed in an attempt to study the growth of new vascular walls on synthetic arterial prostheses. Porous prostheses made from nylon, Teflon, and polyvinyl alcohol sponge were implanted in 45 dogs as a substitute for the abdominal aorta, which had been resected below the origin of the renal arteries. The inserted material was removed for histological examination within several minutes, hours, days, and up to 14 months after the implantation. The specimens, which contained the upper and lower end of the host aorta, the suture area, and the entire prosthesis, made it possible to follow up the entire morphogenesis of the newly formed vascular walls.

The cell-free implanted synthetic prosthesis becomes organized in such a manner that new vascular walls are formed within and outside the prosthesis, and the structural elements of the vascular walls show great similarity to those of normal vessels. The prosthesis itself remains a part of the new vascular walls. Organization takes place from outside by fibrocytes which immigrate from the connective tissue layer of the surrounding area. Transformation of these cells is directed toward the new endothelium and muscle-like elements. The growth of the new endothelial cells is the result of the functional adaptation of the fibrocytes to the mechanical conditions created by the blood stream and the blood pressure. The muscle-like elements which originate from the fibrocytes have fibrils. These fasciculi have a spiral course. There is always satisfactory development of endothelium when the entire prosthetic wall is permeable for cells. In the presence of prostheses which are impermeable to cells, an intimal wedge is formed at the suture site only; this wedge gets thinner after half a centimeter of length, so that frequently endothelial cells are no longer found in the center of the prosthesis. The endothelial cells are considered as a functional form of the connective tissue cells. The transformation of fibrocytes into endothelial cells is emphasized.

The development of a connective tissue framework from the adventitia to the newly formed subendothelial layer is described. In this process the lattice fibers wrap around the muscle-like fasciculi. They present a negative picture of the plasma elements and are functional connective links which are continuous. The blood supply of the new vascular wall develops early in the form of an invasion of capillaries from the old bed of the aorta through the meshes of the prosthesis into the newly formed medium. Emphasis is placed on the new formation from primitive cell material of an organ which is capable of functioning, and the subsequent differentiation of various cell types from primitive connective tissue cells, apparently in adaptation to various functional stresses. The formation of a new vascular wall shows the far-reaching potency of the mesenchyma. Only practical experience will make it possible to decide whether homeoplastic or alloplastic substitutes for the vascular wall are more valuable. Substitution of synthetic substances for arteries is still in the experimental stage, and their clinical use is still limited, despite the fact that a nearly ideal morphogenesis of the vascular wall has been shown experimentally.

Effect of Temperature on Survival of Bacteria in Blood for Transfusion with a Note on Contamination by Cold-growing Organisms. J. D. James and E. J. Stokes. Brit. M. J. 2:1389-1395 (Dec. 14) 1957 [London].

The authors investigated the problem of contamination of blood for transfusion, particularly with regard to the effect of temperature after collection on contaminating organisms. Bacteria which grow at 37 C (98.6 F) and 2 strains isolated from infected blood which grow at 4 C (39.2 F) were inoculated into samples of freshly drawn blood in an attempt to reproduce the actual mode of infection during donation. It was demonstrated that, although experimentally there are slight advantages in refrigerating blood within 30 minutes of collection, in practice refrigeration at the collecting session or during transport to the blood transfusion center in temperate climates is not essential until at least 8 hours after collection. Some samples of blood held at 37 C (98.6 F) for 2 hours immediately after donation killed small numbers of contaminating bacteria; none of the strains tested multiplied in blood during this time.

To prevent contamination of blood for transfusion by cold-growing bacilli, the closed techniques in common use could be improved to prevent the entry of these bacilli in the following ways: The bottle should be autoclaved, with the aluminum cap loose, to prevent the formation of a vacuum, and with the holes in the cap covered by adhesive strapping. The strapping should be removed at the donation session immediately before

bleeding, and the cap should not be touched before the airway needle and the taking-set needle are plunged through it. When the bottle is full, the needles should be removed, still taking care not to touch the cap, which can now be wiped, if necessary, with dry sterile cotton-wool or gauze. The holes should then be sealed with sterile waterproof strapping, and the cap covered with an autoclaved plastic cap. A method is recommended for the examination of blood suspected of infection.

Serum Glutamic Oxalacetic Transaminase (GO-T) in Hepatic and Biliary Diseases. S. Madsen, N. U. Bang and K. Iversen. Nord. med. 58:1008-1013 (July 11) 1957 (In Danish) [Stockholm].

The serum transaminase activity in 41 patients with acute hepatitis was determined by repeated measurements. In the 16 mild cases, transaminase values up to 400-500 units were measured early in the disease, almost simultaneously with the appearance of jaundice. The icterus index was moderately increased. In the 25 more severe cases, transaminase values up to 1,600 transaminase units per milliliter were often seen. Examination of 41 patients with chronic hepatitis and cirrhosis of the liver showed the average transaminase values to be higher in the patients with jaundice. In 21 of the 27 patients with cancer of the liver, the transaminase values were increased; in 6, they were normal. In 6 cases the transaminase test was the only liver test that gave pathological values. In 42 patients with biliary diseases of various origins, the transaminase activity was normal or increased only slightly when there was no evidence of cholecystitis or cholangitis, but it constantly increased in all cases of inflammatory involvement of the gallbladder or bile duct. The serum transaminase test affords some indication of the degree of severity of disease of the liver parenchyma.

Granulomatous Polypi of the Stomach. N. M. Smirnov. Probl. Onc. 3:306-311 (No. 3) 1957 [New York].

The author reports on 21 patients, 10 men and 11 women, between 46 and 55 years of age with granulomatous polypi of the stomach. The duration of clinical symptoms varied from 1 to 20 years. Eighteen patients complained of pain in the underlying region; dyspeptic disturbances of various degrees of severity were noted in 17 patients. All the patients were subjected to x-ray examination, which revealed a single, clearly defined, filling defect of rounded form, situated near the pylorus. Stomach resection was performed in all patients, and one-half to four-fifths of the stomach was removed. Examination of the operative specimens revealed that the granulomatous polypi were situated in close proximity to the pyloric sphincter. Microscopic examination of the specimens showed that the polypi were solitary growths, with the exception of 1 specimen in which 3 polypi were found. The granulomatous polypi presented as nodes with almost unchanged mucous membrane and consisted of precollagenous and collagenous fibers with large numbers of various cell elements, notably eosinophilic leukocytes. Maturation of the granulomatous polypi occurs in the same way as maturation of granulation tissue. No sign of atypia or epithelial proliferation was observed; this finding was in contrast to those in adenomatous polypi, in which such appearances may not uncommonly be observed. Granulomatous polypi can be regarded as a peculiar form of focal inflammation of the gastric mucosa of unknown causation. The 21 cases of granulomatous polypi constituted 20% of all gastric polypi, including also adenomatous polypi with microscopic signs of malignant degeneration, which were observed at the Institute of Oncology of the Academy of Medical Sciences in Leningrad between 1937 and 1953.

Experimental Production of Carcinoma with Cigarette Tar: IV. Successful Experiments with Rabbits. E. A. Graham, A. B. Croninger and E. L. Wynder. Cancer Res. 17:1058-1066 (Dec.) 1957 [Chicago].

After the experimental production of carcinoma of the skin in 3 strains of mice by the application of tar obtained from cigarette smoke, the authors undertook similar experiments on rabbits, animals that have a considerably longer life span than do mice. Cigarette tar was collected in a smoking machine which simulated human smoking habits. The original colony, on which studies were begun in 1951, consisted of 48 rabbits. Seventeen rabbits were added later. The 65 rabbits were divided into 7 groups. Groups A and B were painted with whole cigarette tar. Group B was derived by crossing 2 rabbits of group A in which papillomas developed rather early. It was thought that the progeny might be particularly susceptible to skin tumor induction and that, by further selective breeding, a susceptible strain might be obtained. The results, as far as total tumor formation is concerned, are not significantly different, although the papillomas in group B were, in general, larger and more profuse and appeared earlier. The group C rabbits were painted with a cigarette tar solution from which the basic portions had been removed.

The addition of 1 painting with croton oil per week (group D) did not significantly increase cancer formation, although papillomas appeared somewhat earlier. The rabbits painted with croton oil alone (group E) showed small papillomas, none of which was fleshy or proliferated. It cannot be concluded from this study that the additional application of croton oil had a significant influence on cancer formation among rabbits receiving cigarette

tar. Among the 7 rabbits receiving acetone alone (group F), 5 showed a few small papillomas similar to those in the croton oil group. However, the number of such papillomas was far less than in the croton oil group. Cancer developed in all 4 rabbits painted with 0.3% methylcholanthrene (group G).

The authors conclude that cigarette tar is carcinogenic to rabbit epithelium. Cancer developed in 5 of 41 rabbits painted with cigarette tar on the inner ear, also in 2 out of 10 rabbits receiving an additional painting with croton oil once a week. Four of these cancers were shown histologically to be squamous-cell carcinomas, 1 was carcinosarcoma, and 2 were sarcomas. Removing the basic portions of the tar did not seem to interfere with the carcinogenic activity of cigarette tar on rabbits. Additional application of croton oil seems to have no significant influence on the development of cancer among rabbits receiving cigarette tar.

Hepatitis Epidemic and Serum Transaminase: Serum Transaminase Determinations in Hepatitis Epidemic in Children's Home. N. U. Bang, S. Madsen and K. Iversen. Nord. med. **58**:1013-1015 (July 11) 1957 (In Danish) [Stockholm].

The glutamic acid oxalacetic transaminase activity was followed in the early phases of acute hepatitis and in the mild anicteric cases of the disease in a hepatitis epidemic in a children's home in the fall of 1956. The transaminase activity seems to be a test well suited for the diagnosis of anicteric hepatitis and able to supplement the thymol test which, particularly in children, is not specific. With the transaminase test there is apparently a better opportunity for diagnosis of hepatitis late in the incubation period and a greater possibility for early detection of the subclinical asymptomatic cases. An increased thymol reaction can be the expression of both a present and of an ended hepatitis, and thymol tests alone do not allow distinction between these two possibilities.

Serum Transaminase in Acute Cardiac Infarction. S. Linde and P. Wising. Nord. med. **58**:1018-1021 (July 11) 1957 (In Swedish) [Stockholm].

The serum transaminase activity was increased in 41 out of 43 patients with typical cases of acute cardiac infarction. Thirteen patients died, and the diagnosis was confirmed at autopsy. All the patients with a maximal transaminase increase of more than 300 units died. In only 2 of the surviving patients did the transaminase activity exceed 200 units. The average maximal transaminase increase in the fatal cases was 212 units, while the average in the surviving patients was 114 units. No definite relation between the rise in transaminase activity and the size of the infarction as seen at autopsy was demonstrable.

RADIOLOGY

Roentgen Therapy of Keloids. E. Fischer and H. Storck. Schweiz. med. Wchnschr. **87**:1281-1285 (Oct. 12) 1957 (In German) [Basel, Switzerland].

Roentgen therapy was given to 316 patients with keloids due to trauma, operative wounds, furuncles, trichophytic granuloma, burns, and smallpox vaccination. As a rule, single doses of 400 r were given at intervals of 4 to 8 weeks, and fractionation of these single doses in 3 sessions of 200 r each at weekly intervals was used only for large surface keloids. The total dose, depending on the number of single doses, varied from 800 to 1600 r, and that of the fractionated irradiation varied from 1200 to 2400 r. The duration of treatment varied from 2 to 5 months. Contact or short-distance irradiation with the Chaoul tube was practiced in most of the patients, and the beryllium window-tube, with a tension of 50 kv., was used if irradiation of larger fields was required. Follow-up examinations were made 2-10 years after the roentgen therapy.

Satisfactory results with complete softening and flattening of the tumors were obtained in 83.3% of patients with keloids occurring after operative wounds or trauma and in 58.3% of patients with keloids occurring after extensive burns. Good results were obtained in 75% of the patients who were given roentgen therapy within 6 months after the formation of keloids; chances of success of treatment were only slight when the keloids were of longer standing. Regression of keloids was noticeable at the end of therapy in 65% of all the patients. The best results were obtained with roentgen rays of a half-value layer of 1.5 to 2.5 mm. Al (50 to 60 kv.) with total irradiation doses up to 1200 to 2400 r. In 15 of 292 patients undesired pigmentation and occasional telangiectasia were responsible for a poor cosmetic effect. Surgical intervention is recommended for cicatricial contractions which interfere with function and for keloids of more than ½ to 1 year duration. Roentgen therapy should again be practiced immediately in case of keloid recurrence in the operative scar. Prophylactic postoperative irradiation does not yield better results than x-ray therapy given immediately after onset of keloid formation.

The Definitive Diagnosis of Effusive or Constrictive Pericarditis. L. A. Soloff and J. Zatuchni. Am. J. M. Sc. **234**:687-695 (Dec.) 1957 [Philadelphia].

The authors report on a 46-year-old woman with pericardial effusion and on 2 men, aged 27 and 44 years, with constrictive pericarditis in whom the correct diagnosis was made with the aid of venous angiocardiography or carbon dioxide contrast study. Extraluminal surrounding density due to fluid was the pathognomonic finding of pericardial effusion. A rigid, relatively straight right lateral border of

the right atrium was the pathognomonic finding of constrictive pericarditis. Rigidity of the superior vena cava and of the right ventricle may also be demonstrated. Either diagnosis was supported by the finding of dilatation of the venae cavae, predominantly of the inferior. Effusive or constrictive pericardial disease may be extremely difficult or impossible to diagnose by conventional roentgenologic methods by which the pericardium cannot be isolated from the cardiac shadow and also because all of the cardiovascular derangements produced by pericardial disease, including hemodynamic findings uncovered by the technique of cardiac catheterization, may be mimicked by primary myocardial or endocardial disturbances produced by a variety of diseases. Angiocardiography permits a simple differentiation of pericardial effusion and constrictive pericarditis. Sequential venous angiocardiography allows for analysis of the relative contributions of myocardial and pericardial factors in the production of cardiac disability and permits recognition of myocardial dysfunction. Pericardial effusion and constrictive pericarditis may also be recognized by carbon dioxide contrast study, which is simpler to do although it is not always as effective in identifying with certainty either the presence or the nature of extraluminal change nor does it tell anything of the functional nature of the disturbance.

Late Results of Radiation Therapy for Cancer of the Cervical Stump. R. E. Fricke and D. G. Decker. Am. J. Roentgenol. 79:32-35 (Jan.) 1958 [Springfield, Ill.].

The authors report on 95 women with cancer of the cervical stump who received irradiation therapy between Jan. 1, 1940, and Dec. 31, 1949. Eighty-seven (91.6%) of the 95 patients were successfully followed up. Seventy-four of the 87 patients had true cancer of the stump, i. e., at least 2 years had elapsed between surgical treatment and discovery of cancer of the stump of the cervix. The remaining 13 patients had coincident cancer of the stump, i. e., less than 2 years had elapsed between operation and diagnosis of cancer of the stump, and the malignant lesion had been overlooked at the time of the operation. Fifty (67.5%) of the 74 patients survived for 5 years. The absolute survival rate was 61%. Four (30.8%) of the 13 patients, survived for 5 years. Of the total 87 traced patients, 54 (62%) survived for 5 years; 57% was the absolute survival rate. These results were compared with those in 99 patients with cancer of the stump of the cervix who were treated with radium and supplemental roentgenotherapy between 1915 and 1930 and who were reported on in 1940. Fifty-seven of the 99 patients had true cancer of the stump, and 42 had coincident cancer of the stump. Fifteen (26.3%) of the 57 patients and 9 (21.4%) of the 42 patients survived for 5 years, or 24.2% of the total number of traced patients.

Changes in technique were minor. The marked improvement in results in the patients treated between 1940 and 1949, as compared with those in the patients treated between 1915 and 1930, appears to be due to increased skill of gynecologists and of surgeons in detecting cancer of the cervix before subtotal hysterectomy is decided on and also in earlier diagnosis of cancer of the cervical stump when it does appear. The percentages of coincident lesions and of stage 3 or stage 4 cancers diagnosed were much lower in the present than in the earlier study. The results of treatment for cancer of the cervical stump in the patients treated between 1940 and 1949 compare favorably with the results of irradiation therapy for cancer of the cervix in general, which were reported by the authors in a previous paper, an abstract of which appeared in THE JOURNAL (161:920 [June 30] 1956).

Irradiation of Carcinoma of the Bladder by a Central Intracavitary Radium or Cobalt 60 Source (The Walter Reed Technique). M. Friedman and L. G. Lewis. Am. J. Roentgenol. 79:6-31 (Jan.) 1958 [Springfield, Ill.].

Between 1945 and 1953, 50 patients with carcinoma of the bladder were treated with the Walter Reed technique, entailing a small central source of radium or radiocobalt (Co^{60}) in a proper balloon catheter irradiating the lower two-thirds of the bladder. Twenty-three of the 50 patients had primary lesions, and 27 had recurrent lesions. The lesions varied with respect to anatomic extent (stage) and histological degree of malignancy (grade). The Walter Reed technique necessitates the flexible application of several basic principles to the requirements of each type of tumor if maximum results are to be achieved. These principles are classification of the lesion, cystostomy inspection during insertion of the radiation source, roentgenographic control of the applicator during treatment, fractionation of the dose, serial biopsies, and selection of a suitable total dose for each lesion. The most common dose was 8,000 r gamma in 10 to 17 days, the largest successful dose was 11,000 r gamma in 15 days. Thirty-four of the 50 patients were treated more than 5 years ago, and 19 are alive, an apparent arrest rate of 56%. This unusually high rate will not be maintained because, although the lesions were arrested more than 5 years in 11 of the first 12 patients, the subsequent results were poorer despite increased experience and technical proficiency. The 3-year arrest rate for primary cancer was 65%, and for recurrent cancer 48%. There was no significant difference between the papillary and the infiltrating tumors. Recurrences in the dome of the bladder appeared after treatment with

the Walter Reed technique in 6 patients. Three abdominal wound implants occurred in 35 cystotomies. All were highly malignant, infiltrating cancers.

Success of the Walter Reed technique for the treatment of bladder cancer depends on meticulous technique backed by judgment. Substitution of various radioisotope solutions, that fill the entire balloon, for a central source is much less efficient, with the possible exception of Co^{60} solution. Physically, the latter is somewhat less efficient than radium and has other disadvantages. A standard treatment cannot be employed for the many clinicopathological types in which cancer of the bladder occurs. Results of any technique must be independently evaluated for each category of cancer of the bladder. A scatter diagram, combining the anatomic stage and the histological degree of malignancy, is helpful in classifying cancer of the bladder. There are 2 weaknesses in the Walter Reed technique: a proneness toward recurrences in the dome of the bladder and abdominal wound implants. Some of these recurrences can be arrested with surgery or fulguration. These detractions are minimal compared with the ultimate high arrest rates.

Subcapsular Rupture of the Kidney During Intravenous Urography. M. E. Weiner, F. S. Alcorn and E. L. Jenkinson. Radiology **69**:853-855 (Dec.) 1957 [Syracuse, N. Y.].

Intravenous urography was performed in a 48-year-old woman as part of a general examination. A preliminary film had shown a normal abdomen. There was normal visualization of both renal collecting systems 5 minutes after intravenous administration of contrast material. Subsequently, the patient complained of colicky abdominal pain, and a film made at 15 minutes revealed an unusual collection of contrast material in the right renal pelvis and extending along the capsule toward both the upper and lower poles. At 30 minutes, this extension was increased and there was also some dissection of the medium along the upper right ureter. The impression was that rupture of the right upper urinary tract, probably involving the pelvis, had occurred, with subcapsular extravasation of the contrast material about the kidney and along the upper ureter. A film made 6 hours after injection revealed a nearly complete disappearance of the medium from the kidney area. It was believed to have been absorbed and reexcreted. The pain disappeared and no further symptoms appeared. On follow-up examination approximately 1 year later, the patient was asymptomatic.

The present case is believed to be the first reported example of subcapsular reflux occurring secondary to rupture of the renal sinuses. The pneumatic compressor used in this case was so placed that the lower margin of the rubber balloon was about 2 in. above the symphysis. The balloon is 6 in. in diameter. It is usually inflated to a pressure of between 60 and 80 mm. Hg, with an average compression of 70 mm. Hg. The patient was thin, and the pressure could not have exceeded 70 mm. Hg. It is apparent that the use of external compression may cause sufficient retrograde pressure to produce rupture of the collecting system near its origin and permit subcapsular extravasation of the contrast medium.

A Study of Hodgkin's Disease Treated by Irradiation. M. V. Peters and K. C. H. Middlemiss. Am. J. Roentgenol. **79**:114-121 (Jan.) 1958 [Springfield, Ill.].

The authors report on 291 patients with Hodgkin's disease treated in the department of radiotherapy of the Toronto General Hospital between 1928 and 1954. One hundred fifty-one of the patients gave a history of involvement of the cervical lymph nodes before that of any other site. Only 26 (9%) of the patients showed initial involvement of the more rare sites. The cervical lymph nodes are by far the most frequently noted initial sites of the disease. A study of the 5-year, 10-year, 15-year, and 20-year gross survival rates showed the 15-year survival rate of 25% to be significant because of the moderately large number of 64 patients included in this estimate. Ninety-seven (33%) of the 291 patients failed to survive 1 year. A 10-year survival without recurrence after the initial control is necessary before one can be reasonably confident of a cure, as shown by the year-to-year drop in survival rates. The stage of the disease still ranks first as an important factor in evaluating the prognosis. A significant 10-year survival by stage has now been established as follows: 58% of those with stage-1 disease, 35% of those with stage-2 disease, and 2% of those with stage-3 disease.

A history of symptoms of generalized disease proved to be the second most significant factor determining a poor prognosis, the 10-year survival with this history being 6% as opposed to 60% in the absence of such symptoms. The age of the patient has also an important influence on the prognosis, the best survival rate appearing in the 20-to-30-year age group. The female sex seems to have at least a 10% better prognosis, despite the fact that the disease is twice as prevalent among the male sex. The duration of the disease reflects the chronicity of the disease according to the stage. In general, the patients with early disease of long duration showed longer survivals without recurrence. A plea is made for deliberation and, when necessary, for a period of observation before deciding on the plan of treatment. The survival rates and the incidence of recurrences revealed that there was at least a

35% error in clinical staging. This fact must be borne in mind when initial treatment is planned. Prophylactic irradiation of at least all proximal lymph node regions is estimated to have increased the survival rates at least 20%. Chemotherapy chiefly aided in prolonging the life of selected patients; a possible increase in the survival rates up to 5 years was shown. Pregnancy, particularly after the initial control of the disease, does not appear to alter the prognosis.

Radiation Cancer: A Review with Special Reference to Radiation Tumours in the Pharynx, Larynx, and Thyroid. A. W. G. Goolden. Brit. J. Radiol. 30:626-640 (Dec.) 1957 [London].

Of 24 patients with radiation cancer in the deep tissues of the neck that the author collected from the literature, 18 developed in the pharynx, 5 in the larynx, and 1 in the thyroid. An additional 18 cases of radiation cancer of the pharynx are reported on by the author. Analysis of patients with radiation cancer in the pharynx shows that the relationship between age, sex, and site is similar to that of patients with spontaneous malignant disease of the pharynx, but that an unusually high proportion of patients develop radiation cancer between the ages of 40 and 50. Reasons are given for believing that radiation is likely to prove carcinogenic when other factors which predispose to cancer are present. Radiation cancer of the pharynx occurred after a long latent interval (10 to 35 years, mean 25 years) in patients who received irradiation for thyrotoxicosis or tuberculous lymphadenitis. A few patients did not show signs of severe radiation damage to the skin or subcutaneous tissues. Twelve patients in whom cancer of the pharynx developed after previous irradiation for thyrotoxicosis were seen at Manchester between 1947 and 1954. In this group of patients the observed incidence of cancer of the pharynx was significantly greater than the expected incidence.

It is surprising that so many of the tumors in the deep tissues have been situated in the pharynx while the thyroid seems to be relatively immune to this complication. It is possible that the dose to the pharynx might have been equal to, or even have exceeded, the dose to either lobe of the thyroid in a technique where 2 obliquely inclined fields were directed to each side of the neck. Furthermore, the pharynx is more liable to spontaneous malignant disease than the thyroid. The thyroid is not a radiosensitive organ, though hyperplastic thyroid tissue is more sensitive to the effects of radiation than normal thyroid tissue. It is concluded that the possible development of thyroid carcinoma in patients treated with radioactive iodine for thyrotoxicosis cannot be assessed until long-term survival figures for an adequate number of patients treated by this method are available.

PHYSIOLOGY

Toxicity and Blood Ammonia Rise Resulting From Intravenous Amino Acid Administration in Man: The Protective Effect of L-Arginine. J. L. Fahey. J. Clin. Invest. 36:1647-1655 (Dec.) 1957 [New York].

The author describes studies that were undertaken to demonstrate in man the blood ammonia rise that can develop from intravenous administration of an L-amino acid mixture deficient in arginine, and to confirm the capacity of L-arginine to significantly reduce the blood ammonia changes produced by this mixture. Glycine was also used to produce an elevation of blood ammonia, and the role of L-arginine in preventing this rise was investigated. A marked rise in the ammonia content of the blood and toxic symptoms were demonstrated in patients following the intravenous administration of glycine or an L-amino acid mixture free of L-arginine but complete in all the "essential" amino acids. The rise in blood ammonia appeared to depend on the amount of amino acid and rate at which it is given, the ammonia-forming characteristics of the amino acids infused, and the state of nutrition of the host, particularly in relation to recent arginine intake. The L-arginine was effective in reducing the blood ammonia rise and associated toxicity developing from these intravenous amino acid infusions.

The L-arginine may be given as a part of the infusion or by intravenous injection immediately or some hours prior to the amino acid administration. If amino acid administration and the blood ammonia rise are already underway, injection of adequate amounts of L-arginine will rapidly reduce the blood ammonia rise. The findings indicate that a functioning metabolic pathway requiring L-arginine and consistent with the operation of the Krebs-Henseleit cycle is an important metabolic route when large amounts of amino acids are administered to man.

The Oesophagogastric Sphincter in Hiatus Hernia. M. Atkinson, D. A. W. Edwards, A. J. Honour and E. N. Rowlands. Lancet 2:1138-1142 (Dec. 7) 1957 [London].

Gastroesophageal reflux is the cause of the most disabling symptoms of hiatus hernia, but it is not an invariable accompaniment of hernia nor can the size of the hernia be closely correlated with it. A large hernial sac may be associated with little or no reflux, yet severe esophagitis may occur when the sac is small and inconstant and sometimes even when no hernia can be found. The application of manometric techniques provided a more dynamic picture of the sphincteric mechanism at the esophagogastric junction than was possible by radiography alone. It has shown that interposed between the esophagus and the stomach there is a

short segment in which the intraluminal pressure is higher than the pressure in the fundus. This increase of pressure is brought about by the tonic contraction of a muscular sphincter, which in normal subjects relaxes as an integrated part of the swallowing reflex. Using a similar technique to study patients with hiatus hernia, the authors measured the pressure gradient between the subdiaphragmatic stomach, the hernial sac, and the esophagus. The object was to determine (1) whether the sphincter demonstrable by manometry at the esophagogastric junction in normal subjects is intrinsic or represents external compression by the diaphragm, and (2) whether the occurrence of gastroesophageal reflux is correlated with any particular pattern of pressure gradients between the stomach, the hernial sac, and esophagus.

The authors studied the sphincteric mechanism at the esophagogastric junction by manometry in 7 normal subjects and in 18 patients with hiatus hernia. Evidence was adduced that the sphincteric mechanism is intrinsic and does not represent external compression by the diaphragm. The pressure exerted by the sphincter at the esophagogastric junction constitutes a barrier to gastroesophageal reflux. A measure of this barrier was obtained by subtracting the pressure in the fundus of the stomach, or in the hernial sac, from the pressure in the esophagogastric junction. A correlation was found between the height of this pressure barrier and the presence or absence of symptoms of reflux in patients with hiatus hernia. It is concluded that the tone of the intrinsic sphincter is of cardinal importance in preventing reflux.

Effect of Four Conditions of Cooking on the Eating Quality of Two Cuts of Beef. S. Cover, J. A. Bannister and E. Kehlenbrink. Food Res. 22:635-647 (Nov.-Dec.) 1957 [Champaign, Ill.].

Differences among certain basic cooking methods depend on variations in the temperature and moisture content of the cooking medium. Meat was available from 26 yearling steers of about the same age. They had been fed the same ration under similar conditions. Ten of the carcasses were graded "U. S. Commercial" and 16, "U. S. Good." These steers were from various breeds and crosses. After storage for 7 days, each carcass was divided into the primal cuts and then into 1-in. steaks. Seven steaks from the anterior end of the loin and 5 or 6 from the dorsal end of the bottom round were obtained from each side of each carcass. They were frozen at −20 F and stored at 0 F until tests could be made. Loin steaks were trimmed to include the longissimus dorsi muscle and adhering fat. Bottom round steaks were trimmed to include the biceps femoris muscle and adhering fat. Cuts 1 through 4, numbered from the anterior end of loin and dorsal end of round, were used for tests of eating quality. Paired cuts from the left and right sides of the same animal were cooked—1 by a "moist heat method" (braising) and its pair mate by a "dry heat method" (oven-broiling).

The steaks were cooked to 2 degrees of doneness by broiling (internal temperatures 61 C and 80 C) and by braising (internal temperatures 85 C and 100 C plus a holding period of 25 minutes). The meat was tested for tenderness with a mechanical shearing device and a panel of judges. Scores for tenderness of obvious connective tissue and scores for tenderness of muscle fibers were obtained instead of the usual composite score for tenderness. Juiciness scores decreased with increasing doneness within each method of cooking. The well-done broiled steaks had higher juiciness scores than the well-done braised steaks of each cut and also looked more moist and compact. Shear force values indicated that longissimus dorsi was most tender broiled rare (61 C) but that biceps femoris was most tender braised well-done (100 C and held there for 25 minutes). Thus, severe cooking conditions appeared to toughen the loin steaks but the most severe of the 4 cooking conditions seemed to tenderize the bottom round steaks. Tenderness in meat has more than 1 component, and longissimus dorsi and biceps femoris muscles differ markedly in their tenderness response to certain cooking conditions.

Effects of Posture and Atropine on the Cardiac Output. A. M. Weissler, J. J. Leonard and J. V. Warren. J. Clin. Invest. 36:1656-1662 (Dec.) 1957 [New York].

The factors determining cardiac output in man are incompletely understood. The present study was undertaken to determine the effects of drug-induced tachycardia with the recumbent and upright postures. Atropine was selected as the experimental drug because of its cardioaccelerator effect, which in the recumbent position is associated with little or no alteration in stroke volume. Additional observations were made on modifications of the response to atropine during the peripheral pooling of blood with venous occlusive tourniquets and during anti-gravity suit inflation. The cardiac output response to tachycardia induced by the intravenous administration of atropine sulfate was studied in 12 normal subjects in the recumbent position and in a position of tilt of 60 degrees with the head up. In 4 instances the effects of anti-gravity suit compression on the response to atropine in patients in the tilted position were studied. In 5 subjects the effects of peripheral venous pooling of blood on the response to atropine was also observed.

Significant increases in cardiac output, primarily the result of increased heart rate with little change in mean stroke volume, occurred in patients in the recumbent posture. Only slight elevation of cardiac index, despite even greater tachycardia associated

with a fall in mean stroke volume, occurred with use of the tilted position. Similar results following atropine were observed during peripheral pooling of blood. Sustained anti-gravity suit inflation restored, in part, the cardiac responsiveness to atropine in patients in the tilted position. These data support the thesis that the central venous reservoir is an important determinant of cardiac responsiveness.

PUBLIC HEALTH

A Family Outbreak of Histoplasmosis. I. Clinical, Laboratory, and Follow-up Studies. K. P. Kolb and C. C. Campbell. J. Lab. & Clin. Med. **50**:831-840 (Dec.) 1957 [St. Louis].

The authors report on an epidemic of primary pulmonary histoplasmosis in a family of 4 persons living near Washington, D. C. The father, a 33-year-old man, was critically ill for 3 months, and his 32-year-old wife, a 14-year-old son, and a 27-year-old sister-in-law residing with the family had only mild to moderately severe infections. All recovered. Histoplasma capsulatum was isolated from the sputums of the husband and wife. Elevated titers of agglutinins and complement-fixing antibodies were observed in the serums of all 4 persons, and all the patients had positive results from the histoplasmin skin test. The father was treated with chlortetracycline (Aureomycin), oxytetracycline (Terramycin), streptomycin, aminosalicylic acid, chloramphenicol (Chloromycetin), penicillin, and isoniazid, but none of these agents appeared to alter the stormy course of his disease, characterized by headache, malaise, chills, and fever associated with pain over the right lateral chest. Follow-up chest roentgenograms and skin and serologic tests were obtained 4½-5 years later from 3 of the 4 patients. The roentgenogram of the son showed a typical "snow storm" pattern of tiny calcified nodules, whereas the roentgenogram of the father did not reveal any calcification and no appreciable change in nodular densities compared with that taken 5 years before. The roentgenogram of the wife was negative. Residual complement fixation titers of 1:8 and 1:16 and strongly positive reactions to the histoplasmin test persisted in all 3 persons.

Had it not been for the grave illness of the father, it is doubtful that the milder illnesses of the other members of the family would have been ascribed to any specific agent, much less to the fungus H. capsulatum. The rapid demonstration of agglutinins and complement-fixing antibodies with histoplasma antigens in early serums obtained from each of the patients led to immediate cultural studies. The latter yielded H. capsulatum not only from 2 of the persons involved, but ultimately also from the contaminated chicken compost to which all 4 patients had been exposed, shortly before their illness.

A Family Outbreak of Histoplasmosis. II. Epidemiologic Studies. C. C. Campbell. J. Lab. & Clin. Med. **50**:841-848 (Dec.) 1957 [St. Louis].

The family outbreak of histoplasmosis reported on in the preceding paper was of special interest because it occurred in a geographical area of "low" endemicity and involved persons who lived in a suburban rather than a rural area. Locating the exposure source of Histoplasma capsulatum was complicated by the family's close association with a variety of possible foci. These included decaying wood, birds, their nests and eggs, rodents, domestic pets, and a singular but unrelated incident involving a high concentration of dust. During a follow-up study 4½ years after the primary infections, H. capsulatum was isolated from the dirt floor of an old chicken coop on a nearby farm. The father and son had collected chicken compost from this coop to fertilize the family garden about 10 days before the onset of their infections. The mother and sister-in-law worked in this garden during the next few days. This family outbreak of histoplasmosis comprises only a minor part of the evidence that the District of Columbia area is one of high endemicity for histoplasmosis, contrary to the relatively low prevalence assigned to it on distribution maps. These maps might not be entirely accurate for other regions assigned a low prevalence but where, as in the District of Columbia, the incidence is actually not known, since histoplasmin skin tests—the principal method for determining the distribution of H. capsulatum—have not been carried out with the same intensity in all areas of the United States. The finding of an increased number of cases in any area is generally due to a greater awareness of the disease and improved diagnostic methods. The association of exposure to this organism with commonplace tasks, a possibly increasing number of infections in heterogenous populations of suburban communities, and the prominence of the old chicken coops as a reservoir of H. capsulatum are discussed.

Epidemiology of Syphilis and Factors Which May Influence the Present Tendency Toward Recrudescence. A. Touraine. Presse méd. **65**:1851-1854 (Nov. 16) 1957 (In French) [Paris].

Morbidity reports by public health centers in various countries, which compare the incidence of syphilis of the period 1952-1955 with the period 1943-1947, reveal a decline of the disease of between 66 and 92% in the recent years. The period 1943-1947 corresponds to a period of increase of venereal diseases due to the war. The author believes that a more realistic assessment can be obtained by comparing the period 1952-1955 with the period 1930-1939, when social conditions were more stable. Such comparison would yield a decline of only 26-80%. Another interpretation may be that the fall of reported cases of syphilis in re-

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cent years shows only a short down swing of the secular cyclical trend of this pandemic. The results of serologic tests for syphilis reveal that the decline in number of patients with recent latent and congenital forms of the disease as shown in morbidity reports is smaller than those obtained through clinical evidence. There are indications that the incidence of primary and secondary syphilis has again risen in various countries after 1955 despite extensive syphilis control programs.

Recrudescence of syphilis is due to various individual and general factors. The individual factors are negligence of the patients to seek treatment and occasionally poor cooperation by the physicians to support the venereal disease control programs. On a broader basis, prostitution and incidence of syphilis rise during the periods of economic prosperity, war and population migrations. Foreign workers, jail inmates and clandestine prostitutes are more exposed to the disease than other groups. Certain regions of the world are a sort of a perpetual reservoir of the infectious agent. These reservoirs can be eradicated only through an effective world health program.

Toxoplasma Infections in Animals Associated with a Case of Human Congenital Toxoplasmosis. C. L. Gibson and D. E. Eyles. Am. J. Trop. Med. 6:990-1000 (Nov.) 1957 [Baltimore].

Most of the cases of toxoplasmosis thus far recorded have occurred in newborn infants and undoubtedly have been congenital in origin, since many of the infected infants showed signs of the disease at birth and the mothers gave strong responses when tested for antibodies, although they usually failed to show clinical evidence of infection. The source from which the infection was transmitted to these mothers has not been elucidated, nor is it known where and how the noncongenital infections, either clinical or subclinical, have been acquired. Recognition of fatal congenital toxoplasmosis in a newborn Negro infant in Memphis, Tenn., provided an opportunity for epidemiological study. Serologic tests suggested that all members of the infant's family had been exposed to a common source of infection at a fairly recent date.

Brain tissues from all available animals in the immediate neighborhood were inoculated into white mice in an attempt to isolate Toxoplasma. Parasites were recovered from 7 of 35 cats, from 2 of 3 domestic ducks, from 3 of 7 chickens, from 1 of 16 pigeons, and from 7 of 121 mice, Mus musculus. Of 20 mice caught in the infected family's home, 5 were infected with Toxoplasma, while only 2 of 101 mice from neighboring homes were infected. One dog found 4 blocks away contained parasites, but 8 others taken within a half-mile radius of the patient's home did not. No infections were found in 22 wild sparrows and cardinals. Since all vertebrates in the area, except the wild birds, showed some degree of infection with Toxoplasma organisms, it is suggested that toxoplasmosis should be regarded as a zoonosis in which man is only 1 of several vertebrate hosts.

Vaccination and the Decline in Paralytic Poliomyelitis. E. H. Lossing. Canad. J. Pub. Health. 48:449-453 (Nov.) 1957 [Toronto, Canada].

The Canadian vaccination program began in April, 1955, and by the beginning of the 1956 poliomyelitis "season" some 1,800,000 children had been vaccinated, 90% of whom had received 2 or more doses of the vaccine. In general, the majority of vaccinations were performed in children of primary school age, although in some provinces vaccinations had been extended as well to preschool children and to older children. Comparatively few vaccinations were carried out during the summer of 1956. Knowing that vaccination confers significant protection against paralytic attack but realizing that poliomyelitis is a disease of wide annual fluctuation, it was felt desirable to examine the part that vaccination of this large segment of the younger population may have contributed to the decline in incidence experienced during 1955 and 1956. The percentage distribution of paralytic poliomyelitis in prevaccination years 1952-1954 was compared with postvaccination years 1955-1956 by single year of age up to age 14 and by 5-year age groups from 15 years upward. In the prevaccination years, paralytic poliomyelitis occurred mostly in children in the older preschool and younger school ages, followed by a gradual decline with age, while in 1955-1956 the proportion of poliomyelitis cases among children between 5 and 10 years of age was relatively smaller.

Focusing attention on individual years at the extremes of the period under consideration, a comparison of the percentage distribution of paralytic poliomyelitis by 5-year age groups in the prevaccination year 1952 and postvaccination year 1956 showed a similar picture. In the former, the peak distribution at ages 5-9 followed by a gradual decline with age was evident. When the 1956 distribution was examined, the relative reduction previously seen in the proportion of cases occurring in the school ages was again apparent. The relatively larger proportion of cases in age group 0-4 could be observed. It would seem reasonable to infer that the relative lack of paralytic cases which has been demonstrated in the vaccinated ages is the reflection of the protective effect of the vaccine program. In doing this, however, the possible "natural" immunizing effect of the epidemic year 1953 should not be overlooked. The incidence of paralytic poliomyelitis should be studied over the next few years to ascertain whether further changes in the age distribution pattern will parallel the progressive development of vaccination programs.

BOOK REVIEWS

Stedman's Medical Dictionary of Words Used in Medicine with Their Derivations and Pronunciation Including Dental, Veterinary, Chemical, Botanical and Other Special Terms; Anatomical Tables of Titles in General Use, the Terms Sanctioned by the Basle Anatomical Convention; the New British Anatomical Nomenclature; Nomina Anatomica, Revised by the Fifth International Nomenclature Congress of Anatomists; Pharmaceutical Preparations Official in the U. S. and British Pharmacopeias or Contained in the National Formulary; Biographical Sketches of Figures in the History of Medicine. Edited by Norman Burke Taylor, V.D., M.D., F.R.S.C., in collaboration with Lt. Col. Allen Ellsworth Taylor, D.S.O., M.A., classical editor. Nineteenth edition with etymologic and orthographic rules. Cloth. $12.50. Pp. 1656, with illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1957.

No medical dictionary can hope to keep up with the changes in terminology and additions to the vocabulary in medicine and the allied fields. For this reason frequent revisions are mandatory. A new edition of Stedman's Medical Dictionary, long a classic, was last seen four years ago. That is about as often as a new edition can profitably be published. For those who must use such a dictionary almost daily, a new edition is always welcome and this one is no exception. The names of pharmaceutical preparations have been changed from Latin to English to conform with the latest edition of the United States and British Pharmacopeias. An extensive section on medical etymology is included. Eponyms are defined under the surname rather than under the noun modified (disease, reaction, etc.). Many of the entries are tabular, and some of these include a list of "related terms" that should prove helpful to the student. Appendixes give weights and measures, symbols, proofreader's marks, comparative temperature and barometric scales, chemical elements (this table should have included the common isotopes), pathogenic microparasites (too incomplete a list to be of much value), and anatomic nomenclature. The illustrations are adequate. Unfortunately, in an effort to keep the size of the book—almost 100 pages more than appeared in the preceding edition—within bounds, the type size (the same as in the 18th edition) is very small. How this problem of constant expansion will be met in the 20th edition, promised in three or four years, is hard to foretell, but further reduction in type size would be highly undesirable.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Essentials of Human Anatomy. By Russell T. Woodburne, A.M., Ph.D., Professor of Anatomy in University of Michigan Medical School, Ann Arbor. Cloth. $12.50. Pp. 620, with 403 illustrations. Oxford University Press, 114 Fifth Ave., New York 11, 1957.

This newest textbook of gross human anatomy is characterized by an integrated systematic presentation of the subject under regional headings. Within each region the order of presentation is from superficial to deep, corresponding to dissection procedure. Specific sections on neuroanatomy, embryology, and special senses are not included as detached entities, but the subject matter is included where appropriate in the regions considered. This is a comparatively concise anatomy textbook, yet, as the title indicates, it covers the essentials of human anatomy. The introductory chapter presents the basic concepts of the systems of the body, and succeeding chapters are devoted to the upper limbs, head and neck, back, chest, abdomen, perineum, pelvis, and lower limbs. This arrangement permits the efficient use of this text for almost any variety of dissection sequence. The presentation of variations has been limited to those most frequently encountered, vascular variations being given most attention. The nomenclature used is that adopted in 1955 by the Sixth International Congress of Anatomists. The illustrations help to clarify the descriptive material. Selected references are provided at the end of each chapter. With the present trend toward reduction in time allotted to gross anatomy, a book of this type serves an essential purpose by fulfilling the requirement of conciseness and yet covering the subject with sufficient thoroughness. The volume is well bound, and the type is clear and easy to read. The names of principal structures are printed in boldface type, and cross references are abundant. The quality of the plates is generally good, although some are rather small. This volume can be recommended with enthusiasm for medical students and for physicians who wish to review the essentials of human anatomy.

QUESTIONS AND ANSWERS

HEART DISEASE AND HEMOPTYSIS

To the Editor:—*Three years ago a man, 68 years old, developed what seems to be a typical angina, with substernal pressure brought on by exertion, accompanied by tired feeling along the inside of the arms, and with relief by rest and glyceryl trinitrate therapy. At about the same time he began to have gross hemoptysis, sometimes every day for three or four days. He seems to relate it to his more severe attacks of substernal discomfort, stating that it usually comes on 8 to 12 hours afterwards. Physical examination indicated signs suggestive of aortic stenosis and insufficiency. There is a loud, harsh, high-pitched systolic murmur over the entire precordium. This can even be heard without the stethoscope. It is loudest over the base but also very loud at the apex. There is a thrill in the aortic area, at the apex, and over the carotid artery. The second pulmonic sound is louder than the second aortic sound. There is also a soft blowing diastolic murmur along the left sternal border. Rhythm is regular; blood pressure has ranged from 170/90 to 150/80 mm. Hg. Is there any connection between his heart disease and the hemoptysis? There is no evidence of mitral stenosis. How much diagnostic work should this patient undergo for the purpose of determining the cause of his hemoptysis? Should he have a bronchoscopy, arteriography, etc., when he probably is not a good candidate for anything definitive? Would surgery to improve his coronary circulation be indicated? Would a medical thyroidectomy be of value?* *M.D., New York.*

Answer.—For a connection between the heart disease and hemoptysis, one naturally thinks of mitral stenosis first, which the questioner has done. There may be a mitral lesion associated with the aortic valve involvement, and the physician should energetically and perhaps repeatedly avail himself of roentgenography, roentgenoscopy, and physical examination. Thus, a slightly over-penetrated x-ray film in the posteroanterior view may show the double density of an enlarged left auricle, and the barium-filled esophagus may be indented when viewed in the right oblique position. Failure of the left side of the heart as a cause of the hemoptysis versus a pulmonary etiology could be checked by a circulation time study, e. g., arm-to-tongue time. In heart failure, it would be prolonged; in pulmonary insufficiency, a normal or decreased value would be obtained. Bronchoscopy could be considered, but the bronchoscopist must decide if this man of 68 with an anginal syndrome, hypertension, and valvular lesions could stand the procedure. Aortic insufficiency with failure of the left side of the heart, of course, can induce hemoptysis, but apparently the questioner has excluded heart failure. It is far less common in aortic insufficiency, per se, than in mitral stenosis. Surgery for aortic stenosis has improved, and success has been reported in younger people. If the surgeon attempted this and found a mitral stenotic lesion, he would operate upon both valves. If, however, aortic insufficiency is present, this would complicate the situation considerably and might contraindicate any operative procedure on the valves.

In regard to the question of how to improve the coronary circulation, if the patient is in status anginosus, an intensive medical regimen might improve his condition. Furthermore, the psyche is an important factor, and if one can improve the patient's outlook, he will have a better chance for improvement. Iproniazid, 50 mg., three times daily, after meals, might be assayed. This consultant is giving it a wide trial in angina pectoris, and it is the first drug he has found promising in his whole professional career of nearly four decades. Ligation of the internal mammary artery is a relatively simple operation, and if any procedure is to be performed for the anginal syndrome, this would be the choice. The results, of course, still require longer follow-up. Medical thyroidectomy is also to be considered, and good results have been observed. The candidates, however, were considerably younger than 68 years of age. All in all, a trial of medical treatment at home is suggested, but if the patient is not improved, hospitalization would be essential for further investigation.

EXCESSIVE GROWTH OF BODY HAIR AFTER PREGNANCY

To the Editor:—*What are the possible causes of hirsutism, chiefly of the forearms and face, developing progressively after each of three pregnancies in a 32-year-old woman? What is the treatment?* *Jack Schreiber, M.D., Canfield, Ohio.*

Answer.—Growth of body hair is occasionally noted during pregnancy. This seems to occur more commonly when a familial tendency exists; how-

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ever, it is entirely possible that the growth relates to increase in production of adrenal steroids during pregnancy, which may indeed be responsible for the pigmentation and other changes observed during gestation. Quite frequently the hair growth recedes after delivery, but in those cases where it does not recede, epilation seems to be the only therapeutic possibility.

ANSWER.—Hypertrichosis is found in connection with acromegaly. In such cases the treatment is directed at the acromegaly. It is unlikely that the hair growth would be affected even after the acromegaly has been brought under control—that is, after the progress has been stopped. Hypertrichosis is also associated with hyperfunction of the adrenal cortex, either as in Cushing's syndrome or in the adrenogenital syndrome. In any case, the functional level of the adrenal cortex should be ascertained. Discussion of the various procedures to be used in such a study can hardly be undertaken in this department. It should be remembered that when all other diagnostic procedures have been exhausted, it may still be necessary to do an exploratory operation to determine the size and status of the adrenals.

Cushing's syndrome may be found in connection with adrenals that are the seat of carcinoma or adenoma or in glands that are hyperplastic or entirely normal both macroscopically and microscopically. The syndrome may be treated medically, that is, by the administration of estrogens and other indicated medicaments. This will occasionally bring about a remission, but in such cases the amount of hair does not diminish. To these measures may be added irradiation of the pituitary. This will produce a remission for varying lengths of time in about 25% of the cases. In these cases some hair is lost. Partial adrenalectomy may be done either before or after irradiation of the pituitary. If an adenoma or carcinoma is found, it should of course be removed. Remissions following such a procedure are accompanied by considerable loss of hair.

In cases of the adrenogenital syndrome, administration of cortisone in doses sufficient to reduce the urinary output of 17-ketosteroids to very low levels is the treatment of choice. Recommended doses (Soffer: Diseases of the Endocrine Glands, ed. 2, Philadelphia, Lea & Febiger, 1956, p. 402) as follows: intramuscular injection of 100 mg. of cortisone daily in older children and in adults and 25 mg. daily in infants. After 7 to 10 days the 17-ketosteroid output falls to a minimal level, which should be maintained indefinitely. In general, the intramuscular administration every three or four days is preferable to oral medication. The average maintenance requirement for adults is 75 to 100 mg. every three to four days and for infants 24 to 32 mg. every three to four days. This procedure suppresses the signs of virilism, brings about menstruation, and has some effect on the excess hair. Hypertrichosis is also associated with various tumors of the ovary (arrhenoblastoma, thecoma, and adrenal rest tumors) and also with polycystic ovaries (the Stein-Levinthal syndrome). Exploratory operation may be necessary to determine the structure of the ovaries. Women past the climacteric sometimes grow excess hair and develop diabetes (the Achard-Thiers syndrome or "diabetes of bearded women"). It is probable that the adrenal cortex plays some part in this picture. Finally, in many—perhaps in most—cases, no cause can be found for the excess hair.

PERINEAL PRURITUS

TO THE EDITOR:—*A patient is suffering from persistent perineal pruritus. The urine is negative for sugar. She has no female organ pathology or discharge. Please furnish information as to the possible etiology and treatment.*

Edwin P. Bickler, M.D., Milwaukee.

ANSWER.—Anogenital pruritus in women is most often localized to the vulva or perianal region but may involve the perineum as well. It may occur with or without visible skin lesions. If there are no skin changes except excoriations, the following diagnoses must be considered: (1) psychogenic pruritus, usually due to sexual maladjustment (scratching in these cases often serves as the equivalent of masturbation); (2) menopausal pruritus, which sometimes responds to estrogen therapy and is variously regarded as endocrine or psychogenic; (3) senile pruritus, due to senile atrophy and dryness of the skin; (4) diabetic pruritus, occurring occasionally in patients without glycosuria but with a diabetic glucose-tolerance curve; (5) localized allergic pruritus due to drugs; (6) pediculosis pubis; or (7) pinworms. If the skin is erythematous or shows definite lesions, the following diagnosis must be considered: (1) intertrigo, due to maceration, friction, and poor hygiene, most frequent in the obese and those with hyperhidrosis; (2) irritation due to vaginal discharge or diarrhea; (3) cutaneous moniliasis with or without vaginitis, seen after systemic use of broad-spectrum antibiotics or in diabetics; (4) lichen simplex chronicus; (5) localized manifestation of atopic dermatitis; (6) seborrheic dermatitis; (7) psoriasis, which may be localized to the anogenital region; (8) kraurosis vulvae; (9) contact dermatitis due to soaps, powders, body lotions, underwear, douches, contraceptives, deodorants, antiperspirants, chemicals contained in menstrual pads, toilet paper, nail polish; (10) tinea cruris; or (11) senile atrophy.

Systemic therapy depends on the cause. It includes such measures as elimination of contact irritants, internal allergens, or infectious agents (bacterial, mycotic, or parasitic) and psychotherapy supplemented by sedatives or tranquilizers. Topical therapy depends largely on the condition

of the skin. If there is erosion or exudation, cool astringent sitz baths in 1:40 Burow's solution, boric acid, or camomile extract should be used, followed by hydrocortisone lotion and antipruritic lotions or creams containing 1% phenol, 0.5% menthol, 3% liquor carbonis detergens.

It is best to avoid topical antihistamines and local anesthetics of the "caine" series because of the high incidence of sensitization. If the skin is dry and thickened, Lassar's paste containing 3% Zetar, 2% salicylic acid, and 0.5% phenol is useful. Phenobarbital or antihistamines administered orally have some antipruritic effect. Intravenous injections of 10 cc. of Sandostene with calcium will usually tide the patient over an acute itching crisis. Grenz-ray therapy is extremely helpful in patients with chronic dermatitis. Amino acid ointment should be applied twice daily when there is irritation by soft or liquid feces. For diagnosis and therapy of psoriasis or seborrheic dermatitis in these areas, standard dermatological texts should be consulted. Pruritus not responding to the above measures is sometimes treated by subcutaneous injection of 70% ethyl alcohol (Haskell and Smith: *J. A. M. A.* **106**:1248-1249 [April 11] 1936), resection of pudendal nerves, or even vulvectomy, but even these drastic procedures may be followed by a recurrence of the itching. Vulvectomy is indicated in kraurosis vulvae with extensive leukoplakia. Tattooing of the involved skin with mercuric chloride has given good results in some cases. An excellent and more detailed discussion of this whole problem can be found in Sulzberger and Wolf's "Dermatology: Essentials of Diagnosis and Treatment" (Chicago, Year Book Publishers, Inc., 1952).

AGAMMAGLOBULINEMIA

To the Editor:—*Approximately one year ago a 17-day-old infant was found dead in bed. Gestation and delivery had been uneventful. One year later, a second child was given gamma globulin at approximately 4 weeks of age and was found dead in bed in a manner similar to that of his brother. This may be a matter of coincidence or of gamma globulin disease. Pathological findings in both cases revealed that the individuals died of an interstitial pneumonia. What is the possibility of a similar outcome if there should be a third child? Please comment on the advisability of providing gamma globulin at the time of birth and on maintenance for an indefinite period of time.*

M.D., California.

Answer.—In the infants reported, death occurred at the ages of 17 and 28 days, and pathological studies revealed similar interstitial pneumonias. It might be well to review carefully the microscopic tissue studies to determine if there was anything to point to a common etiological agent to which both infants might have been exposed. The evidence submitted does not warrant the supposition that agammaglobulinemia was present in these patients:

Congenital agammaglobulinemia is a genetic defect transmitted through the mother to male offspring. Suggestive evidence of this disturbance may sometimes be found elsewhere along the family tree. Both these infants were boys, but family history is lacking. Usually, however, in congenital agammaglobulinemia unusual susceptibility to infection is observed only during the second half year of life, after the disappearance of immunity transmitted transplacentally from the mother.

The adult form of agammaglobulinemia is acquired later in life, and women with this disease in the course of pregnancy show increasing levels of gamma globulin during the last trimester. According to Good, this is synthesized in the placenta, not in the fetus, and during this time the mother's capacity for bacterial immunization rises. These mothers do not induce low levels of gamma globulin in their offspring at birth.

Most normal infants, even the offspring of mothers with adult acquired hypogammaglobulinemia, have normal levels of gamma globulin equal to or in excess of those of the adult. During the first few weeks of life the gamma globulin declines in amount and at 2 to 6 months of age may be significantly low. This fact has been advanced by Spain as a cause for the "crib death syndrome" during this age period. The two infants in question, however, died before significant decline in gamma globulin levels would thus be expected to occur.

The injection of gamma globulin under the conditions cited might be of value in possible protection against some common infectious agents, although even large doses will not enable agammaglobulinemic patients to synthesize their own antibodies. There can be no objection to the use of gamma globulin in a future offspring in this family in the hope of thus passively transferring antibodies to it, although this was not successful in the second case recorded. Excellent summaries on this subject are by Good and Zak (*Pediatrics* **18**:109, 1956) and Good and others (*Ann. New York Acad. Sc.* **64**: 883, 1957).

GINGIVAL LEUKOPLAKIA

To the Editor:—*Is there anything that can be done for gingival leukoplakia?* *M.D., Missouri.*

Answer.—Any thickening of the mucosal epidermis tends to develop a whitish discoloration. Leukoplakia is the analogue of senile keratosis on the skin and, as such, has potentialities for malignant change and development. However, in a large number of cases no progression takes place, and in some there is even regression to normal spontaneously or with removal of an irritant such as discontinuance of smoking. Patients using proper

hygiene, who are free of incitants, such as syphilis, may be watched for untoward changes. Thickening, induration, fissuring, and extension of patches should suggest the making of biopsies. Snipping tiny bits of mucosa here and there from selected sites is adequate for histological study. Destruction by cautery or resection is indicated where there is suspicion of irreversible changes. A number of medical measures have been advocated for use both locally and systemically. Unfortunately, none has proved reliable or gives reproducible results.

MONGOLISM AND ADRENAL HYPERPLASIA

To the Editor:—*An 11-year-old girl with typical Mongolism has a history of rather frequent upper respiratory infections, without any serious sequela, and earlier in life had recurrent attacks of pyelitis with none in the past few years. Recently small cataracts have been noted. Growth and development have been about average for this condition. The protein-bound serum iodine level is 3.2 mcg. per 100 cc. Because of the lack of cooperation, a basal metabolic rate determination has never been made. The 17-ketosteroid determination showed 8.1 mg. per 24 hours. The use of 5 mg. of prednisone per day for three weeks reduced the 17-ketosteroid output to 1.5 mg. for 24 hours. When this was discontinued, and after a period of five months, the 17-ketosteroid output was 10.4 mg. for 24 hours. The use of sodium liothyronine, 7.5 mcg. per day, was also tried and helped the character of her skin, and the mother thought that her general vivacity was increased. Except for increase in black hair over the lip areas and over the shoulders, there were no other evidences of virilism. Pubic hair is appearing, as is axillary hair, but this might not be considered necessarily abnormal at this age. The problem is whether under these circumstances there is justification for the continued use of whatever minimal amounts of prednisone are required to reduce the 17-ketosteroid output to normal. Also, in view of the borderline protein-bound iodine level, is the continued use of sodium liothyronine justified?* *M.D., Washington.*

Answer.—In the 11-year-old girl with Mongolism, the depression of the 17-ketosteroid output from 8.1 mg. to 1.5 mg. per 100 cc. after the daily use of 5 mg. of prednisone implies that there is a moderate degree of adrenal hyperplasia. This would explain the growth of hair of the lip, shoulders, and pubic areas. Mongolism is not known to be necessarily associated with adrenal hyperplasia. It would be well to reevaluate the patient's presumed adrenal hyperplasia by determining the 17-ketosteroid level and pregnanetriol level after cessation of prednisone medication. Aside from the cosmetic effect, there seems to be no advantage in continuing the prednisone therapy in this patient. It would be well to continue the use of sodium liothyronine inasmuch as subclinical cases of hypothyroidism are often associated with Mongolism.

SALMONELLA PARATYPHI B

To the Editor:—*Can a definite diagnosis of Salmonella paratyphi B be made without isolating the organism in the blood or feces? A patient's agglutination test was positive and stool cultures were not positive for the organism. Clinically the patient ran a high fever (103 to 104.5 F [39.5 to 40.3 C]) for about four days and had diarrhea but none of the other clinical signs. Please describe the intraperitoneal pathology that would make this condition (Salmonella paratyphi B) simulate acute appendicitis.* *M.D., New York.*

Answer.—For practical purposes a specific Salmonella type of organism cannot be identified as a causative agent of an infection solely on the basis of agglutinins in the patient's serum. A diagnosis of paratyphoid B is not justified in this case in the absence of finding the specific organism. Salmonella paratyphi B may give rise to a typhoid-like disease in man in which there is a bacteremia and involvement of the lymphatics in the terminal ileum. In such cases some of the symptoms may simulate those of acute appendicitis. In the case mentioned multiple blood, urine, and stool cultures should be taken during the course of the acute illness to exclude the possibility of Salmonella. Other infectious agents including enteric viruses must be considered.

TREATMENT OF HIGH FEVER

To the Editor:—*A 2-year-old child has acute tonsillitis with an unremitting fever of 106 to 107 F (41.1 to 41.7 C). Is there any objection to using hormonal therapy (prednisolone, 20 mg. intravenously, or prednisone orally in similar or higher dosage) for a short period to aid in reducing the temperature?*

Milton H. Hollander, M.D., Rahway, N. J.

Answer.—Almost unquestionably most authorities would answer this query with a resounding objection. There is definite objection to relying on prednisone for the treatment of high fever of undetermined etiology at any age. Corticosteroids suppress inflammatory response to infectious agents and disguise clinical evidences of disease. This is employed to good effect in certain well-defined conditions of variable severity—especially in the collagen group of diseases. Suppression of the defensive inflammatory response of the host by means of corticosteroids may lead to dangerous progression of infections due to bacterial agents or even to such mild virus pathogens as varicella or herpes zoster. Probably the dangers in this regard have not been fully explored or anticipated.

In some fulminant bacterial infections, such as bacteremia due to the Neisseria meningitides or the Diplococcus pneumoniae, temporary amelioration of symptoms may be secured by these agents. This expedient is sometimes dramatically effective. This can be utilized with safety, however, only if appropriate antibiotics are simultaneously employed in generous dosage, preferably in excess of those usually given. The use of prednisone in tonsillitis, roseola, or the many other infections of early childhood with which these might readily be clinically confused may lead to a brief and deceptive period of improvement succeeded by progression of the underlying disease unimpeded by the defenses of the patient or the administration of effective anti-infectious agents. Unremitting high fever in a 2-year-old child should first lead to unceasing efforts to determine the exact site of infection and the nature of the pathogen. Once this search is thoroughly instituted, a presumptive diagnosis may point the way to definitive therapy. Meanwhile, purely supportive and symptomatic therapy, aspirin, hydrotherapy, and anticonvulsants are much more useful than prednisone or other corticosteroids and are devoid of the dangers inherent in these powerful drugs.

DERMATITIS HERPETIFORMIS AND NEURODERMATITIS AT THE SAME TIME

To the Editor:—*About five years ago a 15-year-old girl had lesions which were rather typical of a dermatitis herpetiformis. The response to treatment was also typical of the disease. Sulfapyridine helped her tremendously. After some years, the lesions have changed in their distribution. While rather generalized, they involve the flexor surfaces of the elbows and knees. They have a rather characteristic appearance of a generalized neurodermatitis. This time there has been no response to the sulfa drugs. Sulfapyridine was tried first. There was not much response to prednisolone tablets, 5 mg. four times daily. When corticotropin (ACTH), 40 units daily, was given, response was immediate. Sedation with barbiturates was of very little help. Is it possible to have a combination of neurodermatitis and dermatitis herpetiformis? If this is an uncomplicated neurodermatitis, what would be your suggestion as to the management?*

M.D., Alabama.

Answer.—It is possible to have a combination of dermatitis herpetiformis (Duhring's disease) and neurodermatitis in a given patient at the same time. However, dermatitis herpetiformis is characterized by a multiformity of cutaneous patterns, and different aspects may be manifested in succeeding attacks. The lesions of dermatitis herpetiformis may simulate neurodermatitis to a remarkable degree. While there is no reason why a patient could not have dermatitis herpetiformis at one time and a neurodermatitis later, it is just as possible that she had an eruption of dermatitis herpetiformis on both occasions. The treatment of neurodermatitis is difficult. Local application of a 1% hydrocortisone ointment or possibly a tar ointment or tar paint should give good results. Often, tranquilizers are indicated. A starch and soda bath is a good antipruritic agent and is relaxing to the patient. If available, x-ray therapy is valuable. Nonspecific measures such as generalized ultraviolet light and calcium given intravenously are beneficial in many instances. Systemic corticosteroids are indicated only in very severe cases or in those in which more conservative measures have failed.

TESTING FOR FLUORIDE IDIOSYNCRASY

To the Editor:—*Exactly what tests and office procedures can be used to determine individual idiosyncrasy or intolerance to fluorides? Are there practical tests available to the family doctor which he can use to determine whether various subjective complaints are actually caused by fluoride ingestion or just a fear reaction to artificially fluoridated water in a community?—that is, concrete test which may be used to identify early signs of fluoride poisoning, so that a family physician may be guided in his treatment and thereby prevent intractable, neglected cases of chronic fluoride poisoning.*

Herman R. Levine, M.D., Brooklyn, N. Y.

Answer.—What is here asked does not exist. There are no simple tests for blood or urinary fluorides, such as may be carried out by the physician in his office or by the usual clinical laboratory. Precise tests require a high degree of chemical skill and equipment of uncommon nature. In hundreds of instances, these tests have been applied in children and adults prior to the institution of artificial fluoridation, as well as during long periods of properly fluoridated water imbibition, after removal from artificially fluoridated water supply, and in connection with defluoridation of waters naturally high in fluorides. In adults, on initial exposure to fluoridated water the urinary fluoride increases in time and in proportion to the fluoride intake, but a balance is reached after which the output essentially equals the intake. In growing children, the leveling off point is not reached during the growth period, but fluoride retention remains within the limits of tolerance. There is no evidence that the quantity of fluorides thus entering the body leads to any demonstrable indications of harm. This statement does not apply to water consumption when the natural fluoride content is excessive nor to high industrial intake of fluorides. There are no confirmed reports of chronic fluoride poisoning from properly artificially fluoridated waters.

INVOLUNTARY ABDOMINAL MUSCLE CONTRACTIONS

To the Editor:—*A 57-year-old woman for the past six months has been having intermittent, involuntary, spasmodic muscular contractions, which appear to involve the abdominal musculature and which occur principally and regularly in the recumbent position. These contractions are suggestive of hiccups, except that they involve the diaphragm only passively, as demonstrated by fluoroscopy. They occur at irregular intervals of a few seconds and are easily palpable by resting one's hand on the patient's abdomen shortly after she lies down. She has no associated dysphasia, hiccups, or significant digestive complaints. X-rays of the gastrointestinal tract are normal, except for diverticulosis of the colon, which is not causing any difficulty. The patient has taken various tranquilizer drugs, as well as mephenesin, antihistaminics, and quinidine, without result. Please make suggestions regarding diagnosis and treatment of this bizarre phenomenon.*

M.D. Kentucky.

Answer.—The consultant has seen two similar cases. In both there were intense contractions of muscles. In one instance, the contractions were almost exactly as described, making a rippling pattern over the abdomen and over most of the back as well. In the other, the contractions were tetanic and spasmodic and involved the whole lower half of the body and lower extremities. In both instances the disturbances could be clearly related to emotional trauma and were greatly relieved by the intravenous administration of amobarbital. They were thought to represent tonic and clonic muscle contractions as part of a hysterical conversion state.

NARCOLEPSY AND CATAPLEXY

To the Editor:—*A 23-year-old man has narcolepsy, cataplexy, and disturbances of sleep, including somnambulism and sleep paralysis. To control his daytime somnolence, sympathomimetic drugs, thyroid extract, and ephedrine have been used; to all of these he has ultimately become resistant. Please suggest some regimen of medication or routine which could be helpful. Psychotherapy has been considered.*

Frank Anker, M.D., Oakland, Calif.

Answer.—Before psychotherapy is advised, it would be useful to do some laboratory work on this patient. While a number of patients with narcolepsy and cataplexy lack evidence of organic lesion, occasionally lesions of the hypothalamus can produce the same symptoms. Narcolepsy may be a sequela or occur together with encephalitis, brain tumor, polycythemia rubra, and brain injury. Sometimes narcolepsy occurs together with epilepsy.

Spinal fluid analysis, x-rays of the skull, careful and complete blood studies are indicated. An electroencephalogram is of utmost importance. A neurological survey should be of help.

If exhaustive studies are made and there are no evidences of an organic lesion, psychiatric therapy is indicated. Nonorganic narcolepsy is highly resistant to chemotherapy, so that the physician's experience is pretty much universal. Occasionally large doses of amphetamine or methylphenidate hydrochloride will help temporarily, but ultimately one has to get at the underlying cause—organic or not organic—and then treat the cause.

DIET FOLLOWING OPERATION ON LARGE INTESTINE

To the Editor:—*The diet customarily prescribed after operations on the large intestine excludes fiber-containing foodstuffs such as pineapple, cantaloupe, clams, or oysters. What is the rationale of such a regimen? What are the sequelae of breaking such rules?*

M.D., Illinois.

Answer.—Ideas differ widely with respect to the diet indicated after operations on the large intestine. Presumably the question refers to resection of a portion of the colon for cancer or for diverticulitis. In such instances the lesion is removed, and there is no reason for restriction of the diet. If abdominal distress is present there may be other reasons for restricting the diet.

UNUNITED FRACTURE OF RIBS

To the Editor:—*Ten weeks ago a patient suffered a stress fracture of the left first rib at the scalenus attachment. No pathological process existed which could have predisposed the area to fracture or which could interfere with the healing process. There appears to be a nonunion, or at least a delayed union, at present. X-rays to date have confirmed lack of healing. Inadvertent anterior rotation of the shoulder results in a clicking noise and, if repeated several times, leaves the area rather painful, especially at the attachment of the rib to the vertebra. Also, rotation of the cervical spine to the right produces a similar reaction. The literature dismisses rib fractures lightly except for intrathoracic complications but mentions that isolated first rib fractures are rare. What is the recommended treatment and prognosis?*

M.D., Michigan.

Answer.—Ununited fractures of ribs, although rare, are seen often enough to justify the formulation of an opinion about them. The mechanism of fracture usually is one of stress, rather than a direct blow. Violent coughing is one of the most common forms of stress. This probably is why stress fractures of ribs tend more commonly to result in nonunion, for the mechanism of muscle force which originally

causes the fracture in turn tends to cause some displacement of the fragments and excess motion at the site of fracture. Pain is not often a problem when nonunion occurs. If there is pain at the site of fracture, however, injections of hydrocortisone can be tried, and some improvement might be anticipated from this measure. Surgical measures, such as bone grafting, are never recommended. On theoretical grounds, however, rib resection could be carried out as a last resort.

DOUGHY ABDOMEN

To the Editor:—*A 43-year-old woman complains of pains of two weeks' duration over the upper abdomen. Her bowels move three to four time a day. She cannot digest her food and is constantly belching up gas. She gets gas pains in her abdomen at various times, but they are worse after she eats. The gallbladder, with stones, was removed in December, 1954. The abdomen is markedly distended and doughy in consistency. Pelvic examination revealed no tumors or masses or localized tenderness. Stool examination revealed moniliasis. The patient was treated for four weeks with no success. Please advise as to the most effective therapy.*

M.D., Pennsylvania.

Answer.—The most effective therapy will naturally depend upon the underlying disorder. If the impression of a doughy abdomen is correct, then the condition is either tuberculous peritonitis or, more rarely, malignant plastic peritonitis. It may be that a pseudo-doughy sensation was caused by fluid, in which case it would be necessary to differentiate between ascites and a large ovarian cyst by percussion. If ascites were demonstrated, it would be essential to obtain about 10 ml. of the ascitic fluid for specific gravity, total protein, and cytology tests. The diagnosis would follow the investigations indicated by these findings. It is, however, important to suspect the bile ducts in any patient who has undergone cholecystectomy, especially when stones were present. If, in fact, the abdomen is merely bloated with gas and gastrointestinal studies are negative, intravenous cholangiography should be performed to determine the presence or absence of a stone in the common bile duct, which could well account for the findings described.

OPTIC NEURITIS

To the Editor:—*What are the possible causes of optic neuritis, and what is the treatment if one cannot find the cause?*

D. H. Anthony, M.D., Memphis, Tenn.

Answer.—The causes of optic neuritis are so numerous that they can be best classified in groups. The first includes the constitutional diseases, such as syphilis, tuberculosis, sarcoidosis, diabetes, actinomycosis, brucellosis, leprosy, influenza, epidemic cerebrospinal meningitis, typhoid, tularemia, and trichinosis. The second includes local infections of sinuses, intraocular inflammation including uveitis, intracranial infections, infections of teeth and prostate, and gonorrhea. The third includes central nervous infections, multiple sclerosis, acute disseminated encephalomyelitis, neuromyelitis optica, and diffuse periaxial encephalitis. The fourth includes a miscellaneous collection—herpes ophthalmicus, perineuritis optica following tooth extraction, pregnancy, severe hemorrhage, diet deficiency, rarely general malignancy, childhood infections including mumps and whooping cough, thyroid toxemia, and allergy especially to cold. The fifth embraces the hereditary form of optic neuritis (Leber's disease) and toxic drugs or chemicals, of which lead, quinine, benzene, Optochin, hair dye, and sulfonamides are examples. Blood transfusions are seldom a cause. Space is too limited to detail the treatment for each case. A painstaking, time-consuming examination is mandatory, but, while awaiting the exact report, the most probable cause must receive appropriate medication. Steroids have proved of value when there is doubt as to cause.

TOXEMIA OF PREGNANCY

To the Editor:—*Has any relationship between Cushing's syndrome and preeclampsia ever been established? Do patients with preeclampsia have altered ketosteroid metabolism which might be used as the basis of a diagnostic test?*

Donald J. Werner, M.D., Gouldsboro, Pa.

Answer.—No reported instance of Cushing's syndrome and preeclampsia has been found. The majority of patients with Cushing's syndrome in reported series are female; most of these have amenorrhea as a symptom, and they have markedly reduced fertility. Hunt and McConahay (*Am. J. Obst. & Gynec.* 66:970, 1953) reported four women with active, untreated Cushing's syndrome who had a total of seven pregnancies. Hypertension, in varying degrees, was present in all patients, but no mention of albuminuria of more than grade 1 or other evidence of superimposed preeclampsia could be found in records or follow-up. There are no data to validate remarkable ketosteroid metabolism as a basis for the diagnosis of preeclampsia, but there is some change during pregnancy just as there is in other steroids. Recently attention has been given to the measurement of aldosterone in pregnancy and eclampsia (Barnes and Quilligan, *Am. J. Obst. & Gynec.* 71:670, 1956). It is thought that the eclamptogenic toxemias of pregnancy can be grouped with other clinical entities such as cirrhosis, nephrosis, and others which are associated with a fairly consistent appearance of the sodium retaining factor in the urine.

DIABETES FOLLOWING MYOCARDIAL INFARCTION

To the Editor:—*What are the cause and significance of the diabetic manifestations so often encountered after myocardial infarctions in previously nondiabetic patients?*

Walter Newman, M.D., Springfield, Mass.

Answer.—When supposedly nondiabetic persons who develop diabetic manifestations after myocardial infarctions are followed up in subsequent months or years, tests have often demonstrated that the individual really has permanent diabetes mellitus. The suggestion is strong that diabetes was really present in a latent form prior to the coronary occlusion. This situation is particularly frequent when there is diabetes in the patient's family. A number of stressful influences are known to induce glycosuria and hyperglycemia in a person with latent diabetes (prediabetes). These include infection, shock (either surgical or medical, as in coronary occlusion), and endocrine states such as hyperthyroidism. It would appear that diabetes has actually been present in a subclinical or potential form and has simply been brought to the surface by such stressful influences. One recalls in this connection the relatively high incidence of abnormal glucose tolerance made evident by "priming" subjects with cortisone prior to the carrying out of a glucose tolerance test (Fajans and Conn, *Diabetes* 3:296, 1954). Among influences favoring an abnormal result is the presence of diabetes in relatives.

TREATMENT OF PSORIASIS

To the Editor:—*Please give information on the new treatment for psoriasis involving massive doses of vitamin B_{12}.* *M.D., California.*

Answer.—There is hardly a time when new treatments are not recommended for psoriasis. This one, wherein 1,000 mcg. crystalline vitamin B_{12} is injected daily for as long as 30 days, has a few advocates, but it is not generally accepted. The question as to whether or not such large doses have added physiological or pharmacological action is still unsettled. Methods of therapy with riboflavin, inositol, and other vitamins have been recommended from time to time, but they too have not had general acceptance.

GOVERNMENT SERVICE AND A. M. A. MEMBERSHIP

To the Editor:—*Is a physician who has just entered government service eligible to become a service member of the A. M. A.?*

M.D., Washington, D. C.

Answer.—A. M. A. service membership applies only to regular commissioned medical officers and commissioned medical officers of the reserve components on extended active duty with the United States Army, the United States Navy, the United States Air Force, or the United States Public Health Service who have been nominated by the surgeons general of the respective services and the permanent medical officers of the Veterans Administration who have been nominated by the chief medical director. Employees of the United States Civil Service Commission and other governmental agencies are not eligible for A. M. A. service membership and should be reported through their constituent associations. A physician who qualifies for service membership should write to the surgeon general of his branch of service and request that his name be submitted in nomination to the secretary of the A. M. A. A physician who is with the Veterans' Administration, upon request, will be sent an application for service membership, which must be certified by his chief medical director.

CONTINUOUS A. M. A. MEMBERSHIP WITH CHANGE OF LOCATION

To the Editor:—*If a physician moves his practice to a new state and a probationary period is required before application for local society membership will be approved, is there any way whereby A. M. A. membership can be continued during this period?* *M.D., California.*

Answer.—Yes. Chapter II, section 2, of the A. M. A. constitution and bylaws makes a provision for the transfer of a physician's A. M. A. membership from the jurisdiction of one constituent society to another. If the physician has made application for membership in a new state or territorial medical society and a waiting period is required before action is taken on the application, he may continue his A. M. A. membership by sending dues directly to the secretary of the A. M. A. However, this practice can be followed for only two years. If the application has not been processed within this period, the physician's name must be removed from the roster of A. M. A. members.

The suggested procedure for sending dues directly to the secretary of the A. M. A. is as follows: 1. The physician should ask the secretary of his state or territorial medical society to notify the A. M. A. (and send a carbon copy to the physician) that he has made an application to continue membership through his state or territorial medical society but that it cannot be processed before a given date. 2. A. M. A. membership dues should be sent, with the carbon copy of the letter received from the secretary of the state or territorial medical society, to the secretary of the A. M. A. This procedure will permit A. M. A. membership to be uninterrupted.